Psychology and Scientific Research. II. Scientific Inquiry and Scientific Method

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WE HAVE HAD TO DISCUSS the nature of and the apparent reason for scientific inquiry because "scientific research" has so often been thought of merely as a technique or method of investigation. What we know as the scientific method is a means for pursuing scientific inquiry. If we do not bear this in mind, real progress in scientific research is apt to be thwarted. For the implicit equating of scientific inquiry and scientific method to a technique of investigation leaves out an all-important consideration: the problem of formulating a problem for scientific investigation. For the formulation of the problem for investigation must contain within itself the possibility of going beyond what is now scientifically established if it is to satisfy the definition of scientific research. If the formulation of the problem does not do this, then succeeding steps in investigation are futile.

Although there is likely to be little argument here, some "research" in psychology seems to reflect only a lip service to this fundamental tenet. It may be appropriate to underscore the point here in the words of modern scientists. Whitehead has pointed out that "no systematic thought has made progress apart from some adequately general working hypothesis, adapted to its special topic. Such an hypothesis directs observation, and decides upon the mutual relevance of various types of evidence. In short, it prescribes method" (*12*, 286). Einstein and Infeld have written that "the formulation of a problem is often more essential than its solution, which may be merely a matter of mathematical or experimental skill. To raise new questions, new possibilities, to regard old problems from a new angle, requires creative imagination and makes a real advance in science" (*5*, 95). Oppenheimer indicates that the experimental techniques of science enable us to define and detect our "errors of conception" (*9*, 22).

It should be emphasized that if an hypothesis is to be regarded as adequate it must be more than a statement or description of current data and more than a prediction that data will reproduce themselves. An hypothesis must be tested both in terms of its ability to predict immediate events and its promise of leading to further, more adequate hypotheses. For in scientific procedure there is a never ending process of hypothesizing, a constant flow of one hypothesis from another, with each hypothesis trying to go beyond established formulations in its inclusiveness.[1]

It is the way in which the investigator poses his problem that determines where he will come out—what functional activities he will feel have a bearing on the problem, which of these he will use as the bases for standards in empirical investigation, and what methodological procedures he will follow or try to devise. In this connection it is relevant to note that the popular conception of what makes a scientist "great" is that he has solved problems that have long baffled others. While this may be true enough, a review of the history of science will show that in general the solution of a problem is relatively easy once the problem has been posed and that the real scientific contribution of those scientists we now regard as outstanding is due to the way in which they have formulated problems which they or others have solved. The tremendous advances in the physical sciences since the 17th century, for example, are due more to improved formulations than to changes in methodology. In the 17th century and continuing into the 20th, science sought all-inclusive "laws" and felt that reality was firmly in hand. But today both all-inclusive laws and reality seem more elusive than ever. Contemporary physics is seeing its ultimate particle disappear, physiology is realizing that it is not dealing with the classical closed energy system. The need for a basic conceptual reformulation to bring about newer

[1] In a memorandum concerning the conceptualization of novel problems, Horace Fries has called attention to the necessity of making a distinction between an increase in our understanding and the solution of an immediate problem. He points out that "the degree of success in the resolution of the difficulty is always relative, i.e., better or worse relative to the interests or desires affected. But the *solution* of a problem brings about an adequate *resolution* of the difficulty in proportion to the adequacy in which the difficulty is organized into a problem, i.e., the adequacy of the problemization of the difficulty" (*8*).

and greater understanding is apparent on all sides. In his history of science, Dampier-Whetham has noted that "insight, imagination, and perhaps genius, are required firstly to pick out the best fundamental concepts" (*2*, 457).

Search versus research. Much that now passes for scientific research, not only in psychology but in many fields, has precious little to do with what may be honestly called scientific pursuit. But the surface similarity between much current work and real scientific investigation may be sufficient to deceive the investigator himself. If investigators are not to hoodwink themselves and each other and pervert scientific inquiry for some end that has little if anything to do with increasing our understanding of man, it is clearly imperative that they be concerned as consciously as possible with research that will bring about major reformulations. Otherwise they are forced to close their eyes to important problems that face them or to devote themselves only to methodological problems, rationalizing these activities as research.

One variety of this perversion is represented in the shotgun approach, in which the idea seems to be that if one only gathers enough data, possibly with the use of new gadgets or apparatus, one must sooner or later come out with some sort of scientific result. A precedent for this type of activity was set by Francis Bacon who held that "by recording and tabulating all possible observations and experiments, the relations would emerge almost automatically" (*3*, 58). And in the three hundred years since Bacon's time, many investigators have proceeded either without any clear hypothesis or with what they call "limited hypotheses," often so limited that they cannot possibly provide a springboard for further emergence. Much of such data today is concerned with correlational relationships. The situation is such that to an outside observer reviewing the history of modern thought, psychology seems to be merely "trying correlation after correlation in the hope of stumbling on something significant" (*11*, 495).

Another perversion of scientific method is found in the tendency in some areas of psychology to work out elaborate classifications, with the implication that if the behavior of an individual can only be properly pigeonholed in some static system, then further analysis of a functional nature is relatively unimportant for understanding. Karl Pearson's emphasis on classification as a major pursuit of science undoubtedly did a great deal to establish this misconception. One needs only to review the literature in the field of personality or to watch many clinicians diagnose psychiatric patients to see how some men in these areas are struggling to free themselves from older classificatory systems.

Scientific inquiry and scientific method are also not to be confused with investigations limited solely to a so-called "quantitative approach." An overconcentration on problems of measurement as such can easily sidetrack the investigator from the more important concentration on what data are significant to gather and can blind him completely to the problem of problemization, with its concurrent problem of selecting the standards worth measuring. Furthermore, those who are wedded solely to a quantitative approach are all too frequently unwilling to tackle problems for which there are no available quantitative techniques, thus limiting themselves to research impressive only in the elaborate quantitative treatment of data. Current attempts to refine sampling techniques in the field of public opinion research, for example, while indispensable, run the danger of making investigators myopic to certain areas of inquiry that would seem much more important for an understanding or prediction of public behavior—for example, the problem of asking the right questions, of determining the surety of opinion under different circumstances, or the effect of different interviewing situations on response. The current vogue of factor analysis in the study of personality, while most significant as a means of testing a theory as Eysenck's report shows (*6*), frequently reflects insufficient consideration of the relevance or adequacy of the variables thrown into the hopper for analysis.

The function of experimentation and measurement. In saying that what now passes for research (scientific inquiry instrumented by scientific method) is often only scientific pretension, we do not mean to imply at all that reasonable problems for scientific research can be formulated or operated on without including empirical investigation. Experimentation is clearly indispensable as a test of formulation. An hypothesis can be tested only if one is able to do something with it. But it is often forgotten that the value of an experiment is directly proportional to the degree to which it aids the investigator in formulating better problems. And while a single experiment may solve a problem, it can never give us complete understanding. If an investigator believes that by solving a problem he has achieved complete understanding it only shows that his problem has been defined inadequately and is not a step in the constant, never ending scientific search for more and more comprehensive formulations.

The importance of any scientific experiment in which relevant variables are manipulated must be in terms of the breadth of the formulation it has a bearing on. It should be borne in mind that the first and most significant step in experimentation is to determine *if* the variation of one abstracted phenomenon

affects other abstracted phenomena at all. The next most disclosing step is to determine *how* the variation of one abstracted phenomenon affects other abstracted phenomena. We confirm or deny the validity of an hypothesis by determining if and how the manipulation of one variable affects another variable or the total group of phenomena in which we are interested. In the process of using the scientific method of relevant variables, the investigator can discover if and how variables are affected only with reference to some inclusive, higher-order formulation. Otherwise relevant variables could be manipulated forever without making any scientific advance at all. It is also imperative to bear in mind that how much a change in one variable affects another variable does not give us new insight on the "if" and "how" relationship. We determine how much one variable affects another in order to increase our prediction and control, not to increase our range of understanding.

In the process of experimentation, the investigator must be ready to use whatever procedures appear most relevant to an understanding of the problem at hand. These procedures will be both quantitative and nonquantitative. Obviously if we select some phenomenon or characteristic as a variable for experimentation we can do so only because it exists in some degree, some amount, some quantity in relation to the abstracted standard upon which it is based. In scientific research quantitative and nonquantitative procedures are interdependent, and highly refined quantitative investigation may be necessary before one can establish a nonquantitative formulation as, for example, the relationship between the Michelson-Morley experiment and Einstein's formulation. Thus the establishment of any dichotomy between quantitative and nonquantitative procedure is an artificial barrier to scientific progress, separating and taking apart what really belong together in scientific method. Scientific inquiry will be strapped if the investigator feels that he cannot be scientific without being one hundred percent quantitative.

Because scientific methodology is now so often equated solely with quantitative procedures, it may be useful here to distinguish what seem to us to be the function of quantitative procedures in scientific method.

First is the design of controlled experiments or other systematic investigations which involve measurement for the specific purpose of checking a hunch, validating an hypothesis, or testing a general law in a specific concrete situation. As we have already emphasized, the verification of this hypothesis is itself to be regarded only as a stepping stone to further, more inclusive hypotheses. In the fields of psychology and the social sciences, this general function usually translates itself into the purpose of checking some experienced relationships and causalities in an effort to intellectualize and systematize hunches that seem significant.

A second role played by quantitative measurement is the systematic recording of data. But it must be emphasized again in this connection that the accumulation of quantitative results is profitable only to the extent that some previous intellectual excursions have led to an hypothesis which is subjectively held with some degree of surety. Recording without an hypothesis in mind, if it is indeed possible at all, has no place in scientific method.[2]

A third function of quantitative research is to establish norms for the purpose of studying single cases—in psychology, for example, individual or group variations. As any experimental, clinical, or social psychologist knows, quantitative standards are of the utmost importance in predicting how specific individuals or groups of individuals will react in specific situations. But again it must be borne in mind that one undertakes measurement for such purposes only after the formulation of some hunch which may itself be based on nonquantitative evidence. And we must furthermore remember that we can only measure something relative to an arbitrarily established norm.

Whereas most investigators would undoubtedly give a nod of approval to the thesis that quantitative and nonquantitative procedures are interdependent in scientific method, much current work in psychology and the social sciences indicates that in practice this kind of thinking and research-planning is not followed, and that, on the contrary, there is often a conscious or unconscious attempt to imitate the physical

[2] Occasionally Charles Darwin's work has been used as an illustration of the way in which an hypothesis suddenly appears if one can only accumulate sufficient data. But in the famous first paragraph of his introduction to the *Origin of species* (1859), Darwin clearly belies any such contention.

> When on board H.M.S. "Beagle" as naturalist, I was much struck with certain facts in the distribution of the organic beings inhabiting South America, and in the geological relations of the present to the past inhabitants of that continent. These facts, as will be seen in the latter chapters of this volume, seemed to throw some light on the origin of species —that mystery of mysteries, as it has been called by one of our greatest philosophers. On my return home, it occurred to me, in 1837, that something might perhaps be made out of this question by patiently accumulating and reflecting on all sorts of facts which could possibly have any bearing on it. After five years' work I allowed myself to speculate on the subject, and drew up some short notes; these I enlarged in 1844 into a sketch of the conclusions, which then seemed to me probable: from that period to the present day I have steadily pursued the same object. I hope that I may be excused for entering on these personal details, as I give them to show that I have not been hasty in coming to a decision.

And we find in Darwin's letter this further statement (4, 183):

> In October 1838, that is, fifteen months after I had begun my systematic enquiry, I happened to read for amusement Malthus on population, and, being well prepared to appreciate the struggle for existence which everywhere goes on from long-continued observation of the habits of animals and plants, it at once struck me that under these circumstances favorable variations would tend to be preserved, and unfavorable ones to be destroyed. The result of this would be the formation of new species. Here then I had at last got a theory by which to work.

scientists, in the false belief that their success has been due chiefly to the quantitative techniques they have designed. It may therefore be worth a brief historical glance at Isaac Newton's procedure to gain some perspective on the role of quantitative experimentation in verifying and extending nonquantitative observations.

Although Newtonian concepts have been superseded, the Newtonian method remains essentially unchanged and still provides the framework for most of modern science. While Newton's aim was to find absolute, mathematical "laws of nature," his method clearly consisted of (1) simplification and isolation of fundamental concepts, (2) formulation of relevant hypotheses on the basis of these essentially nonquantitative concepts, and (3) intensive quantitative verification and amplification of these hypotheses. Although the concepts of mass and the mutual attraction of gravitation are inherent in a falling apple, it is doubtful if they would ever emerge from a statistical study of *all* falling objects on the face of the globe. As Newton expressed it, "Our purpose is only . . . to apply what we discover in some simple cases, as principles, by which . . . we may estimate the effects thereof in more involved cases." The inverse of this, the attempt to find the "principles" in the welter of "involved cases," would have seemed senseless to Newton.

In developing his methodology, which he nowhere explicitly defines, Newton was in effect systematizing what had become over the centuries the *de facto* method of the "natural philosophers." Nineteen hundred years before Newton, there was sufficient evidence for Aristarchus to advance his heliocentric concept of the universe. This significant concept was, of course, lost until Copernicus, reading the ancients, discovered that some philosophers had "thought the earth was moved." "When for this reason, therefore, I had conceived its possibility, I myself also began to meditate upon the mobility of the earth." The immediate result of this fruitful hypothesis was, of course, a systematic theory which, however, still depended for its acceptance on the principle of mathematical simplicity. Galileo, sensing the importance of experimental verification, provided the last historic step by means of his telescope.

The Newtonian era probably represents one of the most significant and fruitful epochs in human thought. Relevant to our discussion here, the birth of scientific inquiry was accompanied by a formulation of concepts which have determined and dominated thinking up to the present day. Copernicus meditated "upon the mobility of the earth." Newton, age 23, "began to think of gravity extending to ye orb of the Moon." Kepler gave support to the Copernican system because "I have attested it as true in my deepest soul," and "I contemplate its beauty with incredible and ravishing delight." Harvey "began to think whether there might not be a motion [of the blood], as it were, in a circle." Huygens and others formulated the principle of the conservation of what later was termed kinetic energy. The list is virtually endless. In every area of human thought startling and productive contributions were made. Since there is no reason to suppose that the 17th century was especially propitious for the birth of genius, one wonders if the productivity of this period may not be attributed to a fortunate blending of unfettered speculation coupled with a new awareness of the need for empirical verification at every step. Remove the speculation and only barren measurement remains.

Operationism. In the past quarter-century the basic tenets of operationism have so interested all science and have become so ingrained in the thinking of most scientific investigators that no discussion of the role of experimentation in scientific inquiry can be complete without a consideration of the place of operationism which is, historically, a "recent formulation of some of the essential features of the experimental method and of empiricism generally" (*7*, 250).

The impetus for operationism came from Bridgman in physics with the recognition that concepts such as distance have different meanings when used in different contexts. The concept is, therefore, a construct of the observer and not "a thing in itself." It follows that if the variables with which an experimenter deals are products of the experimenter's ingenuity and cannot be specified by pointing to them, then they must be specified by pointing to the procedures employed by the experimenter in creating his constructs. It is only by pointing out the procedures employed in experimentation that the investigator can convey to others the constructs he is dealing with.

Unfortunately, however, the generality of Bridgman's approach has sometimes been lost sight of. There is nothing in the general statement of operationism which delimits or in any way prescribes the defining operation to be used. Bridgman himself has asserted that "any method of describing the conditions is permissible which leads to a characterization precise enough for the purpose in hand, making possible the recovery of the conditions to the necessary degree of approximation" (*1*, 246). Those writers who assert that defining operations must necessarily be "physicalistic" are gratuitously adding a restriction not inherent in the operational approach. This insistence probably trace back to the feeling that physicalistic constructs are somehow more "real" than others and has led to a fundamental misconception and perversion of the operational approach as originally stated.

The inhibiting effect of this artifical restriction has probably not been severe in those sciences more closely

concerned with the physicalistic. In psychology, however, this has tended to exclude the use of psychological constructs and, as Pratt has stated, "to place a stamp of approval on certain limited fields of research in which hypotheses can be neatly formulated in the language of the older sciences" (*10*, 268). We have indicated that a study of relationships alone does not constitute scientific research. Real research must always involve constantly higher-order abstractions. In the field of psychology many of these abstractions cannot possibly be "pointed to" in any narrow operational sense and many of them are not easy to manipulate experimentally. While a scientific investigator must rely upon operational concepts, he must remember at the same time, as Feigl has said, that "operationism is not a system of philosophy. It is not a technique for the formation of concepts or theories. It will not by itself produce scientific results. These are brought about by the labor and ingenuity of the researchers" (*7*, 258).

Selection of standards. A major problem confronting any investigator is the selection or discovery of the standards to use in his investigation. The dictionary defines a standard as "that which is set up and established by authority as a rule for the measures of quantity, weight, extent, value, or quality."

The problem of selecting standards is much more complicated than is often realized, for the reason that the conditional relationships we abstract out of a total situation and except for which the situation would not exist do not themselves exist in their own right. Nor is there any adequate intellectual explanation of their existence. These conditional relationships or aspects of a total phenomenon that the scientist calls "variables" are not God-given and are not limited. Einstein and Infeld point out that "physical concepts are free creations of the human mind, and are not, however it may seem, uniquely determined by the external world" (*5*, 33). Any adjective or any adverb can serve as a potential basis for a variable. Variables that provide the bases for standards are purely the creations of man, enabling him to formulate an abstract, common, determined phenomenal world. The variables employed in any scientific research are based on intuitive judgments and in any concrete investigation depend upon the way in which the investigator has formulated his problem. Since problems are formulated differently in different fields of inquiry, the aspect of a phenomenon that we choose in one field to serve as the basis for a standard in that field will not necessarily be applicable in another field of inquiry. Furthermore, the aspect of a phenomenon that may serve as a basis for standards within any one field will vary according to the nature of the hitch in a concrete situation.

Here words play their familiar tricks even with the thinking of the scientist, who may tend to forget that in his necessary use of word symbols for his thinking and communication (*space, time, I.Q., attitude,* etc.) he is employing abstractions which he cannot, as a scientist, implicitly or unconsciously assume as real in investigation. And it is only to the extent that the investigator is aware of his own transformation of adjectival or adverbial relationships into noun qualities that he maintains the possibility of discovering new conditional relationships except for which a phenomenon would not exist. If abstracted characteristics of the situation are unconsciously reified, complacency or a defensive attitude results.

When we decide on a standard, we take some aspect of a phenomenon, some variable, as a basis for measurement. Since the phenomena with which science deals are so enormously varied, the quantitative units employed in any investigation will depend on the nature of the problem at hand—e.g., distance will be measured in angstrom units or in light years. Also, obviously, we cannot necessarily quantify one standard in the same way we do other standards. While precise units of measurement may be applicable in the physical sciences, in psychology, if we are using some aspect of experience as the basis for a standard, we may have to be satisfied with crude introspective measures such as "more than" or "less than." Whitehead has pointed out that "we must entirely separate psychological time, space, external perception, and bodily feeling from the scientific world of molecular interaction. This strange world of science dwells apart like the gods of Epicurus, except that it has the peculiar property of inducing our minds to play upon us the familiar antics of the senses" (*13*, 62).

Since every standard is based on a man-made assumption, and since it is possible for man to use an infinite number of abstracted subphenomena as bases for standards, the criterion for the selection of what shall be used as the basis for a standard is essentially its usefulness in determining whether or not the abstracted subphenomenon with which we are dealing is constant, verifiable, and potentially helpful in solving our original problem. Also, of course, the basis to be used for our standard must be subject to voluntary recall and to intellectual manipulation.

How do we proceed to select the standards we will use in actual empirical investigation? Since we must start with the nature of the particular hitch we have experienced, abstract generalizations or rules cannot be given. The best that can be done is to describe the apparent functional process that goes on.

It seems to be something like this: In the course of following an acquired interest in understanding why

certain phenomena occur (in physics, biology, psychology, and other sciences) we encounter a difficulty which no previous investigator has resolved to our intellectual satisfaction or perhaps has faced as we face it now. The assumptive world we have built up from experience (which includes the abstracted scientific concepts that have a bearing on the problem) proves inadequate as we try to intellectualize the hitch we have run into. There is no empirical evidence we can find that describes all the conditions except for which the phenomenon that puzzles us would not exist.

In trying to intellectualize the inadequacy of our assumptive world, we discover that a certain condition or set of conditions have not been taken into account. We abstract out of the hitch-situation those aspects we believe are probably necessary to our understanding of the original hitch. We use these aspects of a phenomenon as the bases for our standards, and we vary their "amount." We may have an understanding of why such conditions are important at the time we think of them or we may only have a vague hunch that they are important and may intellectualize them much later. If we have an immediate understanding, we can design our investigation rather precisely. If we have only a hunch, a certain amount of trial and error in experimentation is necessary. But this trial and error takes place within boundaries we set and is not to be mistaken for a shotgun approach. In either case, we design the empirical test of our new basis for a standard with reference to other phenomena that have already been established as bases for standards. We do this in an attempt to determine whether or not the variation in the new basis we have selected for a standard affects old standards and is affected by them according to our formulation.

Our formulation may be validated in some circumstances if the new aspect of the phenomenon we have introduced is affected by other functional aspects. Or, under other circumstances, our formulation may be confirmed if the new aspect we have introduced is not affected by other standards. If our empirical test confirms our formulation and we find that we have abstracted out an aspect of the phenomenon that is the necessary condition for the existence of the total phenomenon, then we can say that we have the basis for a new standard and can proceed to think of it quantitatively.

Once an investigator has discovered new aspects of a phenonmenon that can serve as the bases for standards, it is only too easy for him to slip into the misconception that the particular operation on which he has settled as suitable to the problem at hand exhausts the subject and says all there is to be said about it. This leads to the reification of the very construct which operationism, for example, was devised to avoid. Any science becomes stagnant if it does not regard the discovery of new variables as its primary concern.

We cannot agree with those investigators who believe that the basic variables of all sciences are the same if we can only find them. As we have already pointed out, in psychology this leads to an artificial restriction of the problems dealt with, sometimes to the extent of eliminating from consideration the most pertinent variables. For example, in the attempt to study certain perceptual phenomena, emphasis has been placed on such easily defined variables as "farther than" and "bigger than," where the more psychologically meaningful variable in many cases is probably the subjective feeling of "surer than." If our awareness of a change in an external event is to be considered at all functional in nature, then the subjective sense of surety accompanying the perception must be of primary psychological significance. In the case of those perceptions we label attitudes, investigation of the surety with which attitudes are held under different conditions has lagged far behind our interest in measuring the "direction" of the attitude or opinion.

A note on analysis. The use of the term *analysis* is a poor and misleading way by which to describe the processes involved in determining the variables we will use in our scientific thinking. For analysis assumes the existence of entities existing in their own right which together make up a total phenomenon, and suggests that all we have to do is somehow isolate them, by analysis, for manipulation. Analysis becomes synonymous with the classification of variables in terms of abstracted, fixed, and reified standards.

As we have already indicated, there is an infinity of variables that provide the bases for an infinity of standards. We have said that all adjectives and adverbs furnish a potential basis for standards. And from a study of the history of our language we know that emerging situations bring their own new bases for standards—e.g., the "snafu" of the G. I. When we analyze by using existing standards we make nouns out of adjectival or adverbial relationships often without knowing. For analysis is possible only by using existing standards. Analysis thus does not add anything to our understanding of the functional activities involved in transactional relationships. Hence analysis is not at all similar to what must be regarded as the scientist's constant obligation to discover those aspects of a phenomenon except for which it would not exist. Likewise synthesis—the putting together of that which we have taken apart—is a process by means of which we cannot get any more into the synthesis than is included in the standards made use of in analysis.

The functional activities we pick out for attempted intellectual understanding are those related to the immediate hitch we face. This means, then, that although an infinite number of conditional relationships exist, in any concrete scientific pursuit the range of conditional relationships an investigator might pick out as important will be limited, and will be bounded by the nature of the hitch he has encountered. Scientific progress results from the ability to pick out the most relevant conditional relationships for empirical investigation, not by further analysis of established variables alone.

(This is the second of a series of three articles.)

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Frederick Gardner Cottrell: 1877–1948

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FREDERICK GARDNER COTTRELL, who died at the age of 71, was among those fortunate pioneers who live to see many of their dreams for the betterment of mankind come true. As a scientist, engineer, and humanist, he loved to explore new fields of applied science, to uncover new ideas which his associates might explore and test in detail, to encourage experiments, and to foster projects of promising industrial and social value.

Specifically, he made several important contributions which will be long remembered by scientists and engineers. Among them is the Cottrell electrostatic precipitator, known simply as a "Cottrell," for the precipitation of dust and mist. Also of note are his boiling-point apparatus, the Research Corporation which he established, and the chemical applications of pebble-bed furnaces.

He was a vigorous, unselfish, imaginative physical chemist and industrial engineer who acted something the part of a catalyst in bringing together inventors, engineers, scientists, and industrialists to develop new processes. In these repeated endeavors, Dr. Cottrell had no thought of personal gain or prestige, but was intent upon seeing the wheels of progress turn. He lived modestly, indeed frugally, and cared little about his own comfort. Clothes or traveling accommodations were less important to him than a visit with a productive scientist, or a good book. He read widely and was an indefatigable conversationalist. His abiding interest in people revealed itself in his spoken thoughts. His approach to a group of related ideas or to a new industrial application of science emphasized individual scientists even more than the work they had done. One idea led rapidly to another and in turn to still others, usually by association with names and faces that came to his mind. It was this intense interest in men, coupled with a keen knowledge of the facts and implications of his field of work, that enabled him to accomplish so much.

The broad scope of his interests brought him into early contact with the problem of financing research and development work. With income from patents on the Cottrell precipitator he set up the Research

Corporation, which has since given millions of dollars to support scientific research in universities and private institutions. In 1948 alone, over $750,000 was granted by the corporation for this purpose. Dr. Cottrell was instrumental also in establishing the corporation's policy of helping to put into production commercially important inventions "left on the doorstep" of educational institutions. He worked closely with the Wisconsin Alumni Research Foundation and was a director of the research foundations established at Purdue and Stanford Universities to carry out similar services.

Dr. Cottrell's publications and patents date back to 1906 and relate to many subjects, including the electrical separation of suspensions, cryogenic separation of gases, laboratory apparatus, recovery of wastes, and pebble-bed furnaces.

He was the recipient of many honors: the Perkin Medal, the Willard Gibbs Medal of the Chicago Section of the American Chemical Society, the Medal of the Mining and Metallurgical Society, the Washington Award of the Washington Chemical Society, the Holly Medal of the American Society of Mechanical Engineers, and the Medal of the American Institute of Chemists.

Many different societies claimed him as a member: the National Academy of Sciences, the American Philosophical Society, the American Chemical Society, the American Institute of Mining and Metallurgical Engineers, the American Electrochemical Society, the National Institute of Mining Engineers, the Société de Chimie Industrielle, Phi Beta Kappa, Sigma Xi, and Alpha Chi Sigma.

Frederick Gardner Cottrell, the son of Henry and Cynthia L. (Durfee) Cottrell, was born in Oakland, California, on January 10, 1877. He took his bachelor's degree in chemistry 19 years later at the University of California, spent the following year as Le Conte Fellow at the same university, and taught high school in Oakland for three years before departing for Germany for further study. He obtained his Ph.D. at Leipzig in 1902.

Returning to the University of California, he was instructor there from 1902 to 1906 and assistant professor from 1906 to 1911. In 1911 he joined the United States Bureau of Mines, where he was successively chief physical chemist on field duty (1911–14), chief chemist (1914–15), chief metallurgist (1916–19), assistant director (1919–20), and finally director. Half a year later he relinquished his position as director of the Bureau of Mines to accept the chairmanship of the Division of Chemistry and Chemical Technology of the National Research Council. Within another year, however, in 1922, he was called to head the vigorous and comparatively new U. S. Fixed Nitrogen Research Laboratory, where he felt he could better direct research programs without being restricted so much by administrative detail.

He was director of the Nitrogen Research Laboratory until 1927 and after its reorganization in that year remained as chief of the Division of Fertilizer and Fixed Nitrogen Investigation of the Bureau of Soils in the U. S. Department of Agriculture. Leaving this post in 1930, he continued as consultant to the bureau until 1940. Previously, he had received an LL.D. from the University of California in 1927 and had served as consultant to the Smithsonian Institution in 1928–29.

Perhaps Dr. Cottrell's most exciting period of activity occurred between 1935 and 1938, when he was president of Research Associates, Inc., an organization established to carry inventors' ideas into quick development and application.

In 1939 he persuaded the University of Wisconsin to undertake experiments which might lead to the fixation of nitrogen on an industrial scale. The principle employed involved the application of his pebble-bed method to the heating and quick chilling of air.

During World War II Dr. Cottrell's advice was sought on such projects as industrial use of domestic manganese resources, magnesium production, the manufacture of high temperature ceramics, and many others. By frequent trips around the country he kept in touch with the many researches in which he was concerned. Nominally residing in Washington, D. C., during much of his later life, he spent his final years at Palo Alto, California.

On November 15th Dr. Cottrell was enjoying the company of old friends at the meeting of the National Academy of Sciences in Berkeley on the campus of the University of California, for which he had genuine affection. Among the technical papers he heard was a review of the development of the cyclotron, in which he had been particularly interested and which had been started years before with the help of a grant from the Research Corporation. The next morning, on November 16, 1948, his heart stopped while he was attending a scientific meeting. This is the way he probably would have chosen for the ending of his vigorous, unselfish life.

TECHNICAL PAPERS

Culture of Fruits *in Vitro*

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While culture *in vitro* of plant tissues, isolated roots, stems, and seed embryos has become classical, no reports have yet been made of culture of fleshy fruits after separation of the flower from the plant.

In order to solve this problem, tomato flowers (*Lycopersicon esculentum* Mill.) of the San Jose variety have been cut off from the plant, sterilized with calcium hypochlorite, and planted in Erlenmeyer flasks containing various media. No growth occurred in a medium containing only mineral salts, sucrose, thiamine, and cysteine.

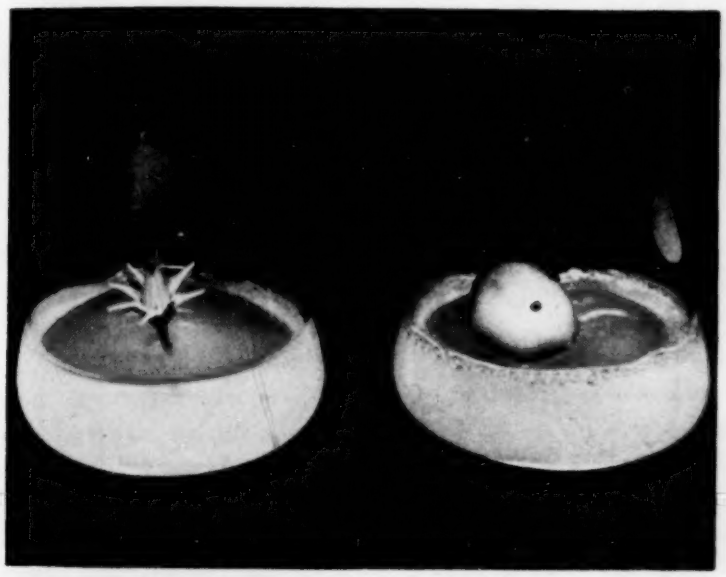

FIG. 1. *Left*, a tomato blossom planted in nutrient agar. *Right*, the tomato which developed one month later. Part of a root is visible on the right of the fruit.

The addition of sterile juice (autoclaved 15 min at 15 lb pressure) from either green or red tomatoes caused the ovaries to develop. A week after planting, the ovaries became visible, pushing up the petals and stamens which had kept them hidden (Fig. 1). The ovaries then enlarged regularly, as shown by diameter measurements, until about the 25th day after full bloom, when growth slowed down. About the 35th day, fruits turned red and ripened at the same time as the controls left on the plant. The growth curve of tomatoes growing *in vitro* (Fig. 2) is in accordance with that given by Judkins (*2*) for tomatoes attached to the plant.

Tomatoes raised from the flower in flasks tasted like usual tomatoes. They were seedless, which might be due either to lack of pollination (the plants were raised in a greenhouse where pollination was very poor) or to killing of the pollen tubes by the sterilizing chemicals. The size

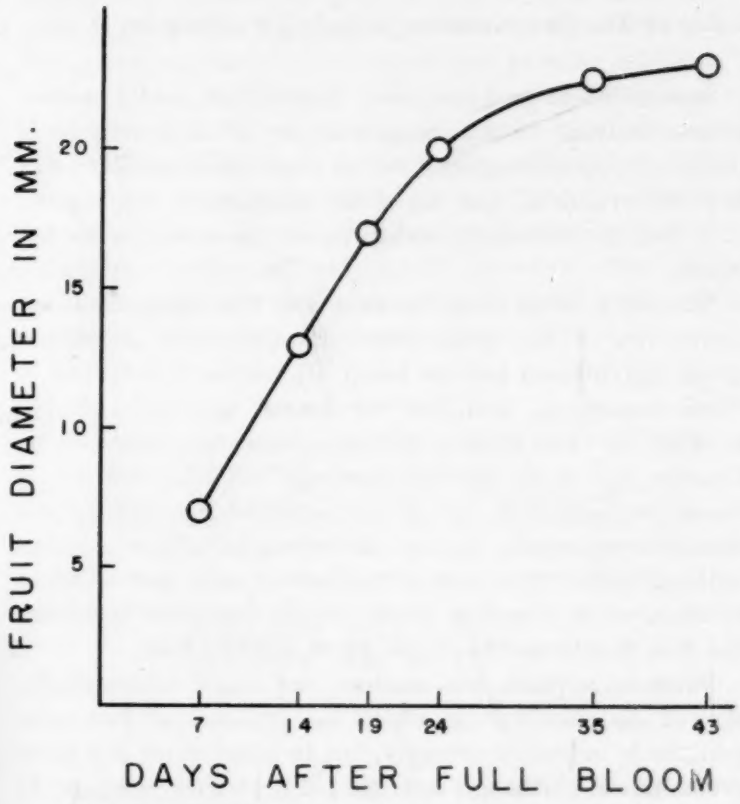

FIG. 2. Growth curve of a tomato grown *in vitro*.

of the fruits was small (about 1 in. in diam), but each flower had only 40 ml of nutrient at its disposal. In some instances, roots developed on the flower stalk; such a fact has been reported only rarely in the literature (*1*).

The factors causing the action of tomato juice on root development and ovary growth were determined by the use of entirely synthetic media. Flowers planted in a medium containing mineral salts, sucrose (4%), vitamin A (1.5 mg/l), thiamine (1 mg/l), riboflavin (1 mg/l), niacin (10 mg/l), and L-tryptophane (10 mg/l) developed roots in the dark but no fruits. The same results were obtained when tryptophane was replaced by α-naphthaleneacetic acid (25 μg/l). Root development was inhibited in the light. On the contrary, using a medium containing mineral salts, sucrose (5%), thiamine (1 mg/l), cysteine (10 mg/l), and β-naphthoxyacetic acid (1 mg/l), small tomatoes were obtained which ripened in the light without the initiation of any roots.

These preliminary results show that it is possible to raise *in vitro* fruits from flowers which have been separated from the plant. Experiments are in progress to obtain full-sized fruits and to cultivate other species by this technique.

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Separating Frequency Distributions into Two Normal Components

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Separation of any frequency distribution into two component normal distributions may be effected readily if either of two assumptions can be made with validity: (1) that the means M_1 and M_2 of the components are known; (2) that the standard deviations of the components are equal.

The only other requirements for the separation are knowledge of the total frequency (or area) N of the given distribution and its mean M, standard deviation σ, third moment ν_3, and, for the second case only, fourth moment ν_4. The method for such separation, outlined by Charlier (*1*) more than 40 years ago but little noticed, is based on Pearson's (*5*) general method for finding two normal components in any distribution, which assumes nothing about them except their existence, and requires solution of a complete ninth degree equation involving the first five moments of the given distribution.

Pearson applied his method not only to markedly skewed distributions, in which the presence of two components is indicated strongly, but to some which are quite symmetrical (although not normal), to find components with identical means but differing standard deviations. His general method applies even when one of the components is negative, i.e., when the given distribution is the difference between two normal ones. This method was used by Crum (*2*) and Pollard (*8*), without reference to De Helguero's (*3*) slight modifications, to Pearson's (*7*) own refinement, or to the simple solutions developed by Charlier for two special cases of great practical significance.

Assumed Means. In obviously bimodal distributions, and many unimodal ones with pronounced "humps" or "shelves," means M_1 and M_2 for two supposed components may be apparent. Their departures from the mean M of the given distribution,

$$M - M_1 = m_1 \text{ and } M_2 - M = m_2$$

were used by Charlier (*1*) to find the variances of the two components (notation simplified):

$$\sigma_1^2 = \sigma^2 - 2m_1m_2/3 - (m_1^2/3 + \nu_3/3m_2)$$
$$\sigma_2^2 = \sigma^2 - 2m_1m_2/3 - (m_2^2/3 - \nu_3/3m_1).$$

The total areas or frequencies of each component depend only on the assumed means:

$$N_1 = Nm_2/(m_1 + m_2) \qquad N_2 = Nm_1/(m_1 + m_2).$$

Finally, from a table of normal frequency curve ordinates, $\phi\ (t)$, the ordinate at any distance (in t units) from the mean may be found, since

$$y_1 = (N_1/\sigma_1)\ \phi\ (t).$$

The larger component always corresponds to the smaller departure from the mean, which in turn is m_1 if ν_3 is positive, m_2 if negative. Should impossible means be assumed for the two components, σ_1^2 or σ_2^2 will be negative, indicating no real solution.

However, the method of assumed means does not give a unique solution: usually trial of several pairs of means is required to find one set yielding two components which, added together, closely approximate the given distribution. The best pair of means generally has maximum ordinates agreeing well with the observed values, due regard being given to the contribution each component makes to the other's peak. Such agreement can be made

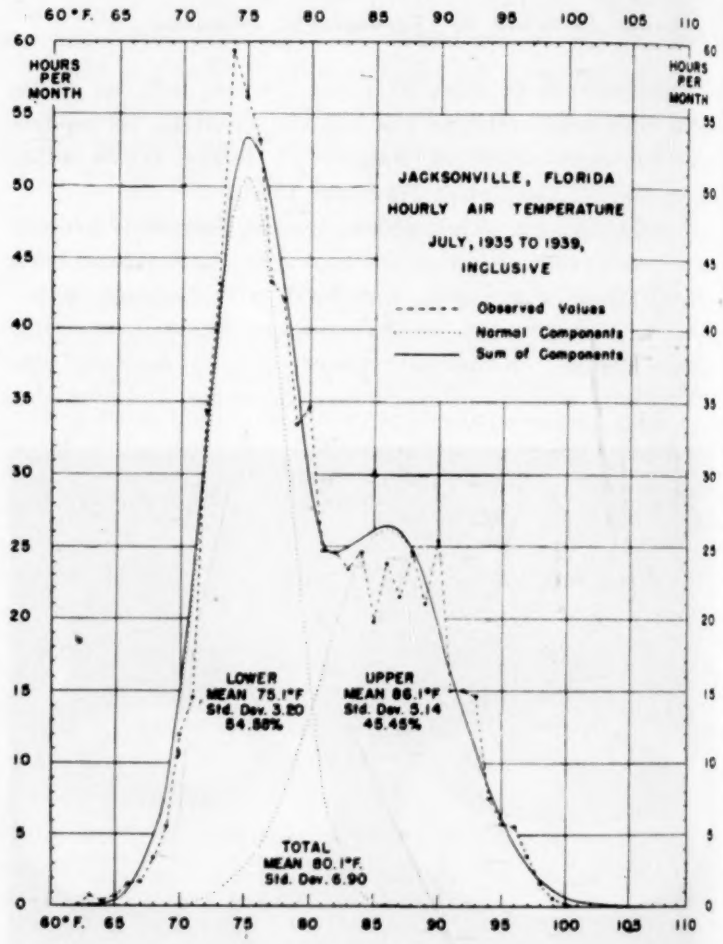

FIG. 1.

as close as desired by assuming values of the maximum ordinates y_1 and y_2 in addition to the means M_1 and M_2. Then

$$\sigma_1 = N_1/\sqrt{2\pi}\, y_1 \quad \text{and} \quad \sigma_2 = N_2/\sqrt{2\pi}\, y_2.$$

Example. Charlier's method of assumed means (without assuming values for the maximum ordinates) has been applied (Fig. 1) to 3720 hourly temperature readings during July at Jacksonville, Florida; significance of the two components found by this method will be discussed elsewhere. In the data, even temperatures are disproportionately more frequent than odd ones, because observers, required to estimate readings to tenths of a degree, tended to values ending in 0.0 or 0.5; the latter, by the classic rule for disposal of decimals, then were rounded to the nearest even degree. If, instead, all 0.5 values were rounded to the *next higher* units, frequency distributions would be smoother and means too high by only 0.05°.

For these Jacksonville data, several pairs of assumed means were tried and discarded before two finally were found yielding components whose sum (Fig. 1) seems a

reasonable approximation to the original curve. A still better fit might have been obtained from means differing from the given mean by tenths of a degree, instead of by the half-degree intervals fixed upon to simplify computations.

Equal standard deviations. Assuming the two presumed components to have equal standard deviations, instead of assuming values for their means, led Charlier (*1*) to a cubic equation involving the difference between the variances of the given distribution and the assumed components:

$$z^3 + \tfrac{1}{2}(\nu_4 - 3\sigma^4)z + \tfrac{1}{2}\nu_3^2 = 0,$$

where $z = \sigma_1^2 - \sigma^2$. The discriminant of this cubic,

$$C^2 = (\sigma^{12}/216)\ (13.5\alpha_3^4 + E^3),$$

where $\alpha_3 = \nu_3/\sigma^3$ is the skewness and $E = (\nu_4/\sigma^4) - 3$ the excess, almost always is positive, indicating only one real root:

$$z = 0.4082\ \sigma^2\ (\sqrt[3]{-3.6742\alpha_3^2 + \gamma} - \sqrt[3]{3.6742\alpha_3^2 + \gamma}),$$

where $\gamma = \sqrt{13.5\alpha_3^4 + E^3}$.

Except for almost symmetrical and very flat-topped distributions, γ is positive, so that z will be negative, and

$$\sigma_1^2 < \sigma^2.$$

But if $-z > \sigma^2$, then σ_1^2 is negative, and there is no actual solution, indicating the assumption of equal standard deviations to be unwarranted; for Jacksonville July temperatures, variances assumed to be equal are -5.07.

If the assumption is justified, and σ_1 is real, the means are:

$$M_1 = M - m_1 = M - (\nu_3/6) - \sqrt{(\tfrac{1}{4}\nu_3)^2 - z}$$

$$M_2 = M + m_2 = M - (\nu_3/6) + \sqrt{(\tfrac{1}{4}\nu_3)^2 - z}.$$

The areas N_1 and N_2 of the two components are found as before.

An asymmetrical curve which is the sum of two normal curves "affords a good fit both to distributions which possess two distinct modes, and to skewed distributions with one mode" (*8*). That components have not been found generally for such distributions may be due to ignorance of Charlier's facile methods; this ignorance, in turn, may stem from Pearson's insistence (*6*), replying to Edgeworth's criticism (*4*), that his "process is not so laborious that it need be discarded for rough methods of approximation based upon dropping the fundamental nonic and guessing suitable solutions."

Of Charlier's methods, the first, that of assumed means, is far simpler than the second, which involves the fourth moment and a cubic equation. However, Charlier concentrated on the second, the "abridged method for dissecting frequency curves," because the cubic equation involved is actually one step in the general solution, "hence it is no loss of time to begin with this approximate method."

Charlier declared that the assumption that the standard deviations of the two components are equal "is of a more general character" than the assumed knowledge of the means of the two components. "Especially in biology it is a fairly probable supposition that two types found together in nature often possess *nearly* equal standard deviations," but "this abridged method is applicable only when there are a priori reasons for the assumption that the two components have nearly equal standard deviations." In many cases no such reasons exist, and then it is safer to assume certain values for the means of the components, especially when approximate means may be determined by inspection. In the example given, the approximate values of the means were obvious from the graph, and trial of a few pairs of values yielded one which gives a good fit, with markedly different standard deviations; assumption of equal deviations gave no solution.

Even closer agreement with the original distribution can be obtained if values may be assumed for the maximum ordinates as well as the means of the two components. In effect, this short cut replaces the standard deviation and skewness of the original distribution by a subjective evaluation which may be more effective for some distributions, but is not of as general applicability in finding two normal components.

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Combination of Tissues from Different Species in Flask Cultures[1]

Clifford Grobstein and J. S. Youngner[2]

National Cancer Institute, Bethesda, Maryland

Combining tissues from different species apparently has been performed only infrequently in tissue culture. Roffo (*5*) grew together chicken and rat tissues, both normal and neoplastic, without evidence of antagonism. In studies of the mode of transmission of the excitation involved in cardiac muscle contraction, several investigators (for reference see Leone [*3*]) combined embryonic heart fragments of the chick with similar fragments from other avian and mammalian species. The establishment of synchrony of beat was reported, and no mention was made of any incompatibility reactions.

Harris (*2*), in an attempt to determine whether direct incompatibility exists between tissues of different mammalian species in culture, paired heart, spleen, and kidney fragments from newborn mice and rats in roller tubes. Harris found that ". . . rat and mouse tissue cells are physiologically compatible *in vitro*." In a related study, though not involving tissues from different species, Medawar (*4*) recently made combined fluid cultures of skin from two adult rabbits, between which skin grafts had failed to take, and found no evidence of incom-

[1] With the technical assistance of Clara Lee and Edward J. Soban.

[2] Present address: Department of Bacteriology, University of Pittsburgh Medical School.

patibility. The present report confirms these earlier observations, in that no overt incompatibility has been found in combined cultures of tissues from mouse and rat, mouse and guinea pig, and mouse and chicken, even when the mouse tissues were derived from animals previously immunized against the opposite species.

TABLE 1

SUMMARY OF MOUSE-RAT TISSUE COMBINATIONS

Mouse (strain C)	Rat (strain Marshall or Hairless)	Duration of experiment (days)	Total number cultures
Kidney, 16-day embryo	Kidney, embryo, near term	6	2
" adult	" adult	6	2
Spleen, 16-day embryo	Spleen, embryo, near term	6–11	5
" adult	Kidney, embryo near term	6	2
" "	" adult	6	2
" "	Spleen, "	6	1
			14

All cultures were carried in modified Carrel D-3.5 flasks. Aseptically prepared tissue fragments, 1–2 mm in diam, were planted several millimeters apart in a clot of 0.6 ml chicken plasma and 0.8 ml of a nutrient fluid consisting of 2 parts horse serum,[3] 2 parts Tyrode's solution, and 1 part chick embryo juice. After the clot formed, 1.0 ml of the nutrient fluid was added to each flask. Three times weekly the nutrient was drawn off, the cultures were washed with 2.0 ml of Tyrode's solution, and fresh nutrient added. In some cases (see Tables 2 and 3), the chick embryo juice was omitted from the nutrient in order to slow the rate of growth.

Tables 1–3 list the various tissue combinations studied. Strains and ages of donors are given in the tables. Omitted are the controls which were run in each experiment and which consisted of cultures of paired tissue fragments from one species—either mouse, rat, guinea pig, or chicken.

Early contact of individual cells, as well as the later stages of growth, was observed microscopically. At intervals, representative cultures were photographed and, in some cases, fixed and stained, using a modification of the technique of Earle (*1*).

To determine whether immunization of one species against antigens from another affects the reactions of their tissues when combined in culture, groups of young mice (5–7 weeks old) were injected with either guinea pig serum (diluted 1: 7 with saline), guinea pig kidney (brei diluted 1: 10), or chicken serum (diluted 1: 3). The immunization course consisted of intraperitoneal injections twice weekly for 3 weeks. The total amount of diluted antigen given was 4.5 ml. One week after the final injection the mice were bled, along with controls, and the desired tissue taken for culture. Pooled serum samples were tested for antibody content by the "ring" precipitin test. Antibody titers of 1: 64 in the anti-guinea pig sera, and 1: 640 in the anti-chicken serum.

TABLE 2

SUMMARY OF MOUSE-GUINEA PIG TISSUE COMBINATIONS

Mouse (strain C)	Guinea pig (family 13)*	Duration of experiment (days)	Total number cultures
Kidney, 16-day embryo	Kidney, embryo, near term	4	3
Spleen, 16-day embryo	Kidney, embryo, near term	4	1
Spleen, 16-day embryo	Spleen, embryo, near term	4	2
Spleen, adult	Spleen, adult	5	3
" "	Kidney, young, 7–9 days	11	5
" " †	Kidney, young, 7–9 days	11	6
" " ‡	Kidney, young, 7–9 days	11	6§
Lymph node adult	Kidney, young, 7–9 days	11	11§
Lymph node adult†	Kidney, young, 7–9 days	11	11§
Lymph node adult‡	Kidney, young, 7–9 days	11	5§
			53

* Inbred line developed by Dr. Sewall Wright and maintained by Dr. Walter Heston at this institute.

† Donor mouse immunized with guinea pig serum.

‡ Donor mouse immunized with guinea pig kidney.

§ Chick embryo juice omitted from nutrient fluid in one half of cultures.

TABLE 3

SUMMARY OF MOUSE-CHICKEN TISSUE COMBINATIONS

Mouse (strain C)	Chicken (stock)	Duration of experiment (days)	Total number cultures
Kidney, 16-day embryo	Heart, young, 7–9 days	21	9*
Kidney, young, 7 days	Heart, young, 7–9 days	21	9
Spleen, 16-day embryo	Spleen, young, 7–9 days	4	2
Spleen, young, 7 days	Heart, young, 7–9 days	21	9*
Spleen, adult	Kidney, young, 7–9 days	4	3
" "	Heart, young, 1 day	8	9
" " †	Heart, young, 1 day	8	9
			50

* Chick embryo juice omitted from nutrient fluid in one half of cultures.

† Donor mouse immunized with chicken serum.

[3] Kindly supplied by Dr. Wilton R. Earle.

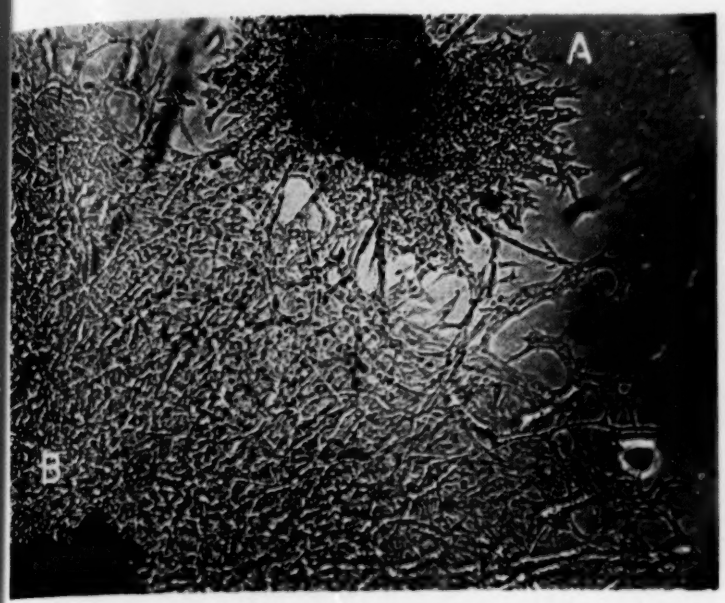

FIG. 1. Four-day combined culture of (A) spleen of mouse immunized with chicken serum, and (B) 1-day-old chick heart. Note that outgrowth zones have joined and that there is no evidence of antagonism. Magnified 90 ×.

During the first few days of incubation, extensive cellular migration occurred from all explants. In cultures of tissues from different species, cells at the margins of the outgrowth zones came into intimate contact with each other (Figs. 1 and 2) as in cultures of tissues from the same species. In both types of culture, the cells in the contact zone, as elsewhere, appeared normal. The cells were observed to come together in the contact zone and, as migration continued, the margins of the outgrowth zones were joined without any sharp demarcation. There was no evidence of: 1) abnormal cellular accumulation or reaction along the line of junction between the two explants, 2) altered rate or direction of growth in the contact area, or 3) specific attraction or antagonism between cells of the two species. Once the growth zones joined, continued cultivation with or without embryo juice, up to a maximum of 21 days, produced no further change, apart from progressive growth of the cultures.

The growth patterns described were identical in the case of combinations involving explants from previously immunized animals. Tissues of immunized mice, as compared with those of nonimmunized mice, showed no difference in reaction to tissue fragments from the species that furnished the antigens.

The results show that tissues of two different species, as widely diverse as mouse and chicken, may be grown simultaneously in flask culture without apparent antagonism. This is true even when the donor mouse has been previously immunized against antigens of the species furnishing the other tissue of the paired combination, and when the mouse tissue is one which *in vivo* presumably is intimately involved in antibody formation, i.e., spleen and lymph node. At present, the chief significance of these findings is seen in the possibility that such combined cultures may provide a method for investigations requiring maintenance of healthy tissues of two species in close physiological relations.

Further investigation is necessary before these results may be interpreted in relation to problems of antibody production *in vitro* and of incompatibility in transplantation *in vivo*. Interpretation at present is hindered for the following reasons: First, no attempt was made to provide optimum conditions for antibody production, or its detection in the culture fluids. Second, the media used contained components heterologous for both species, thereby complicating immunological interpretations. Finally, in the present state of knowledge of cellular physiology in culture, it is not safe to transfer directly to the organism conclusions based upon observations of cellular behavior *in vitro*.

FIG. 2. Four-day combined culture of (A) lymph node of mouse immunized with guinea pig serum, and (B) 3-day-old guinea pig kidney. Intimate contact of normal cells from the two species can be observed. Magnified 280 ×.

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Transphosphorylation by Alkaline Phosphatase in the Absence of Nucleotides[1]

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Axelrod (*1*), using citrus fruit phosphatase, observed the transfer of phosphate from nitrophenyl phosphate to methanol in the absence of nucleotides. The transferred phosphate did not pass through the inorganic stage. Recently, we observed with alkaline intestinal phosphatase a strong acceleration of the rate of synthesis of glycerophosphate from inorganic phosphate and glycerol, in the

[1] This work was aided by grants from the American Cancer Society, recommended by the Committee on Growth; the Division of Research Grants and Fellowships of the National Institutes of Health; and the Rockefeller Foundation.

presence of biological compounds with phosphate bonds of higher energy than glycerophosphate (*2*).

It has since been established that this acceleration is achieved in the absence of nucleotides by a direct phosphate transfer, that is, without passing through the intermediary stage of inorganic phosphate. When a mixture of P^{32}-labeled phosphocreatine, synthesized enzymatically (*3*), unlabeled inorganic phosphate, and glycerol was incubated with intestinal phosphatase at 38° C for 15 and 30 min, the glycerophosphate in excess of that synthesized in the absence of phosphocreatine (representing two-thirds to three-fourths of the total glycerophosphate) had about the same specific activity as the phosphocreatine, while the specific activity of the inorganic phosphate was quite low. If the phosphate transfer had passed through the intermediary stage of inorganic phosphate, then the specific activity of the glycerophosphate synthesized could not be higher than that of the inorganic phosphate. Similar results were obtained with radioactive phosphocreatine, fructose, and inorganic phosphate: at the end of 15 min of incubation more than half of the total fructose-phosphate formed derived its phosphorus directly from the phosphocreatine. Other observations indicate that phosphopyruvate glucose-1-phosphate (and similar compounds with relatively high phosphate bond energy) can also participate as phosphate donors in such a direct phosphate transfer.

TABLE 1

SPECIFIC ACTIVITIES OF THE PHOSPHATE SPECIES IN THE PHOSPHORYLATION OF GLYCEROL AND FRUCTOSE AT 38° C WITH PHOSPHOCREATINE LABELED WITH P^{32}

	Initial molar concentration	% Acceleration of synthesis	Specific activity cpm/γ P	
A			0 min	30 min.
Phosphocreatine	0.0252		1090	895
Inorganic P	0.448		0	9.3
Glycerol	1.63		–	–
Glycerophosphate	0.0	290	0	606*
B			0 min	15 min
Phosphocreatine	0.030		1828	1750
Inorganic P	0.444		0	13.3
Fructose	2.34		–	–
Fructose-phosphate	0.0	375	0	730*

* Corrected for the nonlabile P impurities present in the phosphocreatine preparation.

In Table 1 the specific activities (cpm/γ P) of the different phosphate species from two such experiments are given. The general composition of the enzymatic incubation mixture was the same as previously reported (*2*).

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Hatching Eggs of Floodwater Mosquitoes in Media that Promote Plant Growth[1]

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In a natural environment, eggs of floodwater mosquitoes are deposited on soil, in debris, or among plants in places subject to transient submergence. In such sites they remain in a viable state for a year or longer, and usually hatch when they are flooded with water at a proper temperature. However, submergence in this manner is not a dependable provocation for hatching eggs of these mosquitoes in the laboratory, according to numerous observers. Water in natural habitats must contain stimulants to hatching that are not found in tap water. Several observers have noted that durable eggs of the genus *Aedes* may be stimulated to hatch by infusions made from plants that grow in the natural oviposition sites and by cultures of bacteria and yeasts. Abdel-Malek (*1*) found that eggs of *Aedes trivittatus* Coq. hatched erratically in dilute solutions of chemicals that regulate plant growth such as 1-naphthaleneacetic, 3-indoleacetic, and 3-indolebutyric acids. No one seems to have devised a way to get eggs to hatch in consistently high percentages in a few hours, as occurs in nature.

Larvae of floodwater mosquitoes hatch after two phases of growth have been completed in the egg. The first is an increase in number of cells, which continues until the fully formed embryo occupies all of the interior of the egg. The second is an increase in size of the embryo, until the shell of the egg is ruptured. Between the two periods, eggs may be dormant for months. Temperature regulates the rate of increase of cells, and the nature of the solution surrounding the eggs has much to do with initiating escape of the larvae. The final act of hatching involves an increase in size of the embryo in a manner similar to the elongation phase of growth of plant tissue. Media that stimulate one might affect the other similarly.

Eggs of the floodwater species, *Psorophora discolor* (Coq.) may hatch at any time after the embryos are fully formed. Maturation of the embryo requires about 4 days at a temperature between 22 and 26° C. If kept on a moist surface at a temperature within this range, larvae may hatch whenever the eggs are submerged in a suitable medium. Eggs kept on a moist substratum at a temperature of 15–20° C in the laboratory have survived and yielded vigorous larvae after at least 9 months. However, prolonged exposure of eggs to temperatures as low as 15–20° C will prevent any medium from causing hatching until the eggs are conditioned for several days at a temperature favorable for hatching.

Substances that promote growth of plant tissues vary in effectiveness. Thimann (*3*) states that short sections of etiolated oat coleoptiles will elongate slightly in water, more in water containing purified growth-promoting sub-

[1] Contribution No. 290 of the Department of Entomology, University of Illinois, Urbana.

stances, and vastly more when sugar is added to the medium. He further states that a suitable medium for the purpose of growing plant tissue contains sucrose 1%, potassium chloride M/100, and indoleacetic acid 1–5 mg/l. Caplan and Steward (*2*) have shown that dilutions of milk from ripe coconuts, and corn lyophilized while in the milk stage contain factors that stimulate growth of carrot explants many times more than purified indoleacetic acid alone. The purpose of this paper is to show the order of increasing influence of various types of media on the hatching of eggs of a common species of floodwater mosquito, *Psorophora discolor*.

Preparations for observing the effects of various media on the rate of hatching of eggs were carried out in the following manner. Solutions were prepared by dissolving the ingredients in tap water without sterilization. Some were used as soon as they were prepared, and others were aged at 20° C for periods of time shown in Table 1. All solutions of glucose and sucrose contained 10,000 ppm of the sugar. Potassium chloride was used at the concentration of 7460 ppm. Indoleacetic acid, in all solutions containing sugar, was used at a concentration of 5 ppm; otherwise dilutions were as shown in the table. Acetic acid and ethyl alcohol were used in concentrations of 100 ppm. The extract of canned corn (used in lieu of lyophilized corn) was composed of the turbid filtrate from a mixture of 1 part of cream-style corn in 4 parts of water. Coconut milk was diluted to 5% of normal. The yeast suspension consisted of four pellets of living dried yeast dropped into a tube of tap water containing the eggs. Eggs were submerged in the media, and records were made of the number of larvae hatched after 4 and 24 hr. Some media caused hatching for 48 and 72 hr, but no data are included for intervals longer than 24 hr. All eggs were stored on moist cellucotton for 4–5 months at 15–18° C and conditioned for 10 days at 26–27° C before submerging them.

Hatching of conditioned, durable eggs of *Psorophora discolor* was stimulated by substances that effect plant growth, as is seen in Table 1. Tap water alone had hardly any effect on the process when eggs had been conditioned only 10 days. Purified substances, when used in concentrations of 2–10 ppm, stimulated 36–43% of the eggs to hatch within an interval of 24 hr, but they were ineffective during the first 4 hr. Similarly, solutions containing glucose, when freshly prepared, caused no hatching within 4 hr, but within 24 hr 57–71% of the eggs were hatched. Diluted fresh coconut milk and a freshly prepared extract of commercially canned cream-style corn caused hatching of 80–82% of the eggs. The last two media caused most hatching within 4 hr.

Aging of all solutions containing sugar advanced the time of hatching so that nearly all eggs hatched within 4 hr after submergence. However, the total number of eggs hatched was less in all aged media (with one exception) than was the case with relatively sterile coconut milk and extracts of canned corn. The exception was the aged medium containing glucose and indoleacetic acid, which caused as high a percentage to hatch as rapidly as those containing coconut milk and corn extract. Aged media containing ethyl alcohol were inferior to others in ability to stimulate hatching. Only 19% of eggs treated with media containing alcohol hatched within 4 hr, and 58% hatched within 24 hr.

Media containing sugar were suitable for development of certain bacteria and yeasts, and these may have added

TABLE 1

INFLUENCE OF VARIOUS MEDIA ON THE HATCHING OF LARVAE FROM EGGS OF *Psorophora discolor* IN THE LABORATORY

Medium	Age of medium	Eggs treated	Larvae hatched					
			0–4 hr		5–24 hr		Total	
	days	no.	no.	%	no.	%	no.	%
Extract of canned corn	0	120	93	77	5	4	98	82
Coconut milk (5%)	0	330	243	74	21	7	264	80
Glucose, KCl, and indoleacetic acid	2–7	180	137	76	2	−1	139	77
Glucose, KCl, and acetic acid	3–5	240	141	59	21	9	162	68
Glucose, and acetic acid	2–3	180	107	60	11	6	118	66
Glucose, and ethyl alcohol	3	260	49	19	102	39	151	58
Sucrose, KCl, and indoleacetic acid	0	20	0	0	98	81	98	81
Glucose, KCl, and acetic acid	0	180	0	0	127	71	127	71
Glucose, KCl, and indoleacetic acid	0	180	0	0	116	64	116	64
Glucose, and acetic acid	0	90	0	0	52	58	52	58
Glucose, and KCl	0	90	0	0	53	59	53	59
Glucose	0	180	0	0	102	57	102	57
Indoleacetic acid (5–10 ppm)	0	60	0	0	26	43	26	43
Indolepropionic acid (2–10 ppm)	0	70	2	3	24	34	26	37
Indolebutyric acid (2–10 ppm)	0	70	0	0	25	36	0	36
Yeast suspension	0	40	0	0	5	12	5	12
Indoleacetic acid (0.1–2.0 ppm)	0	250	1	−1	13	5	14	6
Acetic acid (20–100 ppm)	0	300	6	2	4	1	10	3
Indoleacetic acid (20 ppm)	0	30	3	10	0	0	3	10
Tap water	0	340	4	1	2	−1	6	2
Potassium chloride	0	30	0	0	0	0	0	0

some stimulus to hatching. Yeast alone in tap water provides no stimulant for hatching that is very effective within 24 hr. The suspension used caused no hatching within 4 hr and very little within 24 hr. Therefore yeast alone is not likely to have added a stimulant to the aged media containing sugar that brought about hatching within 4 hr.

Durable eggs of *Psorophora discolor*, when submerged in media that promote growth in plants after a proper period of conditioning, hatch in a manner analogous to the elongation reaction of plant tissue. Water alone permits little or no hatching; purified stimulants cause less than half of the eggs to hatch; sugar in the medium may favor microorganisms that shorten the interval between submergence and hatching and increase percentage of hatch; freshly prepared extract of commercially canned cream-style corn and dilutions of coconut milk hasten hatching and increase the number of larvae hatched.

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A New Apparatus for Recording of Ecologic and Climatic Factors, Especially Temperature

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For many purposes it is of interest to know for what length of time the temperature has been above a certain point, e.g., 0° C. A recorder that can supply this information may be constructed using the following principle.

If a ray of light of constant intensity illuminates a photographic plate, and the plate after a certain period is removed and developed, the degree of darkness will be a function of the time during which the plate has been illuminated. If the illuminated spot moves as a function of temperature, and such an apparatus is placed under varying temperatures, one may, after a certain period, remove and develop the plate. By photometry of the picture thus obtained, one may tell something about which temperatures occurred during the time of exposure, and the frequency of occurrence of each temperature.

A paper impregnated with a salt of a radioactive element of sufficiently high stability, e.g., a salt of radium, supplies a constant source of radiation that affects a photographic plate.

On this principle, the apparatus shown in Fig. 1 has been constructed.

A pointer (4) is connected with a bimetal strip (2) which bends with temperature. At the tip of the pointer, a metal plate is placed, and through this a slit (5) is cut. The slit is 1 cm long and consists of two parts, an outer one 0.5 cm long and 0.4 mm wide, and an inner one 0.5 cm long and 0.2 mm wide.

The system of bimetal strip and pointer is fastened in a metal case (1). The pointer moves parallel to the lid of the case (6).

The lid seen from below is pictured in Fig. 1 c. There is a frame (7) with two springs (8). In this frame a photographic plate is fastened so that two sides of the plate are pressed towards two sides of the frame. Thus the photographic plate is placed in a known position.

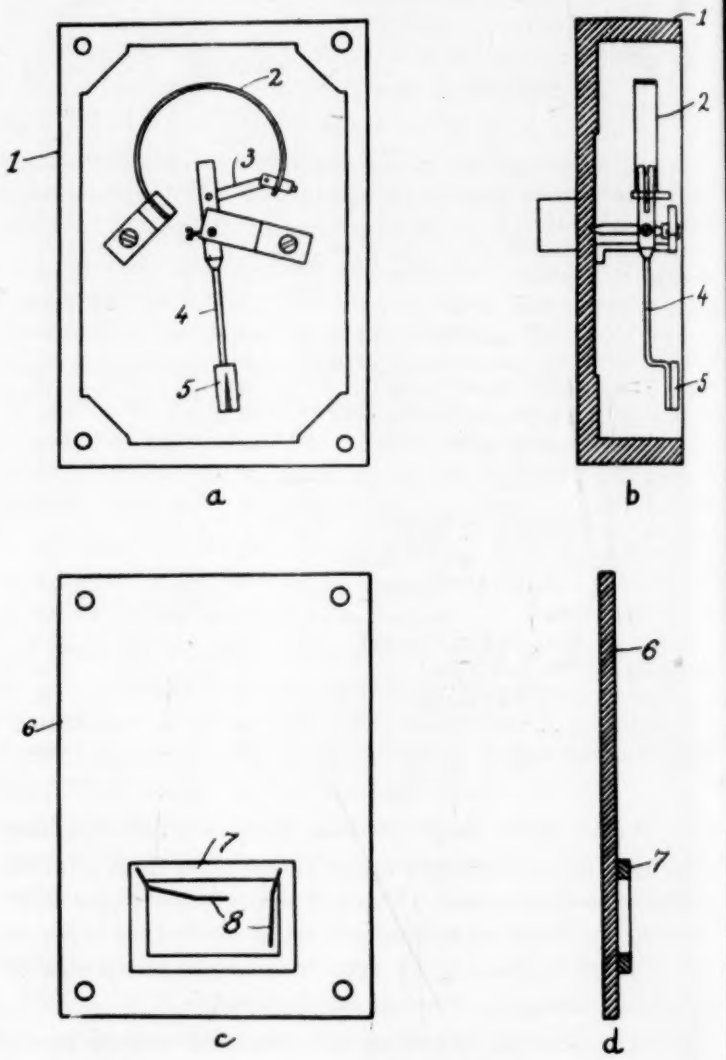

FIG. 1.

On the under side of the slit, a piece of paper impregnated with radium sulfate is fastened. Only the α- and β-particles going through the slit can reach the photographic plate. Some of the γ-rays going through the metal plate will reach the photographic plate, but if a fine-grained type of plate is employed, the photographic effect of the γ-rays is negligible in comparison to the effect of the α-particles.

When a photographic plate is placed in the frame, the lid fastened to the case, and the apparatus left under varying temperatures, different parts of the plate will be exposed to radiation at different temperatures. Each time a certain temperature occurs, one definite sector of the plate will be exposed, and in the course of time the exposures will be superimposed and added.

When the plate is removed and developed, and a photometric curve is made across the "spectrum" thus obtained, it is possible to calculate from it which temperatures occurred during the observation period, and the part of the observation period during which the temperature was higher than a given value. To obtain such results certain points must be taken into consideration:

1. A suitable photographic plate must be chosen. It should be fine-grained and should not change its properties even during long observation periods. The Agfa Normal Diapositive Plate serves this purpose.

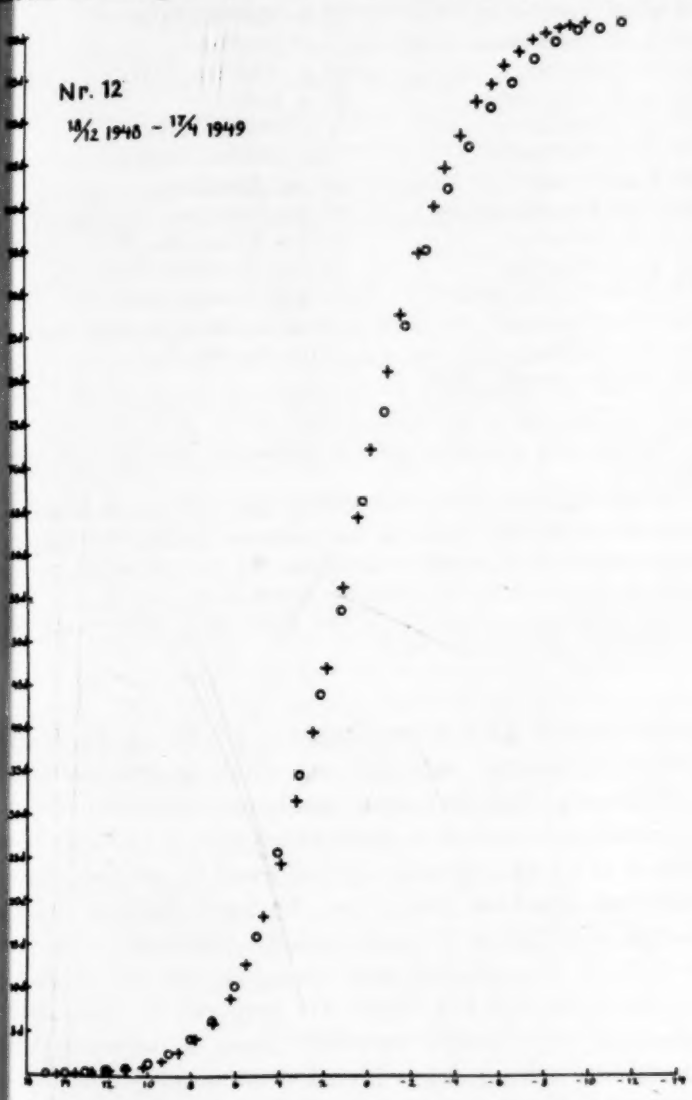

FIG. 2.

2. A suitable balance between the observation period, the activity of the radioactive paper, and the sensitivity of the plate must be found. For recordings of over one year an amount of approximately ½ γ radium sulfate/cm² was found suitable.

3. The relation between the time of exposure and the degree of darkening of the photographic plate must be found. The relation is very closely linear when a fine-grained plate is subjected to radiation by α- and β-particles even at low intensities.

4. The sensitivity of the plate as a function of temperature must be found. An experiment gave a sensitivity increase of 8% when the temperature was raised 23° C. This is an error for which correction must be made.

5. A standard exposure at definite temperatures must be made and photometric curves must be taken in the same way as in the original plates, to know which sectors of the plate correspond to which temperatures.

6. Because the slit has a certain width, the photometric curves give only an approximate representation of the relationship between the temperatures and the frequency of occurrence of each temperature interval, an error for which a correction must be made.

As a test, some of the apparatus was left for a certain period in the observation hut of the Norwegian Meteorological Institute at Blindern, Oslo, where continuous recordings with thermographs are made. From the thermograph curves the same factors may be calculated as from the photometric curves.

One of the results is given in Fig. 2. The ordinate shows number of days with temperatures higher than that given on the abscissa. Circles represent values calculated from the thermograph curves; crosses, values calculated from the photometric curves. The correspondence is good.

It will be evident that the same principle, although only with approximation, may be employed in all factors where the records can be transferred to the movement of a pointer, e.g., humidity, barometric pressure, etc. However, one does not know at which temperatures the exposures were made, and errors due to differences in the sensitivity of the plate with temperature cannot be corrected for. This difficulty may be overcome by making the width of the slit variable. If one side of the slit is fastened to a bimetal strip, this may be arranged so that the width of the slit decreases at higher temperature to compensate for the differences in sensitivity of the plate. Thus the same principle may be applied over a wide range of ecologic, climatologic, and other types of instruments.

A more detailed description and discussion is found in *Physiologia Plantarum*, 1949, 2, 272.

Cup Assay with Vitamin B_{12} as a Standard

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The cup assay method proposed by Heatley (*1*) for the estimation of penicillin has several advantages over standard turbidimetric or titrimetric procedures. Chief among these is the adaptability of the method to routine handling of large numbers of samples from a variety of sources. Evaluation of reproducibility of the method and discussion of factors influencing it have been presented by Heatley (*6*). The requirements for satisfactory microbiological assay methods have been listed by Foster and Woodruff (*4*).

Assays for biotin, thiamine, and riboflavin (*2, 5*) by the cup assay technique have been described. The factors crucial for antibiotic cup assays apply equally to the determination of growth-promoting factors by the cup method.

The microbiological estimation of LLD (*L. lactis* Dorner) type activity by means of *Lactobacillus lactis*,

or by means of *L. leichmannii*, using vitamin B_{12} (*10*) as a standard, is influenced by degree of aeration, by oxidation-reduction potential, and by accumulation of peroxides. These factors are difficult to control in the titrimetric assay procedure (*8*, *9*). The cup technique has allowed more rigid control of influential factors, with a resulting assay of much greater precision. Also, by use of abnormal salt concentrations, it has been possible to eliminate the diffuse growth response of the test culture to desoxyribonucleic acid or to its constituent nucleosides.

The constituents of the medium described for the Merck modification (*3*) of the Shorb titrimetric estimation of LLD activity (Table 1) are combined as a dry mix and milled in a hammer mill or ball mill, in an area of low humidity. This milled ingredient dry mix is incorporated in the assay medium to give the final composition as shown in Table 1.

TABLE 1

Item	Amount
Milled ingredient dry mix (See Table 2)	22.9 g
Spray-dried HCl-hydrolyzed casein*	1.0 g
Adenine, guanine, and uracil solution†	10.0 ml
Sodium chloride‡	20.0 g
Agar	20.0 g
Distilled water	To 1 l

* Prepared by refluxing Sheffield high nitrogen casein with 20% HCl for 20 hr, then passing the hydrolyzate through a bed of an anion-exchange resin to neutralize the excess acid, and finally spray-drying it.

† Solution contains 1 mg/ml each of adenine sulfate, guanine hydrochloride, and uracil in distilled water, acidulated with just enough H_2SO_4 to maintain the ingredients in solution.

‡ Added in order to eliminate growth response to desoxyribonucleic acid, thymidine, or reducing substances.

This assay medium is sterilized by autoclaving 20 min at 120° C, in 1-liter quantities, which may be combined to yield sufficient medium for assay of all the samples accumulated on a single day. The medium, without adjustment, is at pH 6.2 after sterilization.

An alternate medium, which is less expensive for routine assays, may be prepared by incorporating 20 g L-cystine, 20 g DL-tryptophane, 10 g DL-aspartic acid, 20 g DL-α-alanine, and 20 g ammonium acetate in the dry mix, in place of the 18 amino acids listed in Table 2. For each liter of final medium, 20.1 g of alternate mix and 2 g of spray-dried HCl-hydrolyzed casein are required. Additional supplements are added, as in the previously described medium. Although growth response is adequate from the alternate medium, it is preferable to use the complete mix whenever possible, rather than to rely on the variable composition of casein preparations as a source of essential amino acids.

Inoculum is prepared by 18-hr incubation of *L. lactis* Dorner A.T.T.C. No. 10,697[1] in the assay medium without agar and NaCl, but supplemented with 0.0001 μg of vitamin B_{12} per ml. Five ml of the inoculum culture,

[1] Kindly supplied by Dr. Shorb, University of Maryland, College Park.

TABLE 2

INGREDIENTS FOR DRY MIX FOR CUP ASSAY*

20 g DL-Isoleucine	1000 g Dextrose
20 g DL-α-Alanine	600 g Sodium acetate
20 g L-Cystine	50 g Fumaric acid
20 g DL-Aspartic acid	50 g Sodium ethyloxalacetate
20 g DL-Norleucine	20 g $MgSO_4 \cdot 7H_2O$
20 g L-Tyrosine	1 g NaCl
20 g DL-Valine	129 g $Na_3PO_4 \cdot 12H_2O$
20 g DL-Methionine	67 g K_3PO_4
20 g DL-Glutamic acid	1 g $FeSO_4 \cdot 7H_2O$
20 g DL-Threonine	1 g $MnSO_4 \cdot 4H_2O$
20 g DL-Serine	20 mg Riboflavin
20 g DL-Phenylalanine	20 mg Calcium pantothenate
20 g DL-Leucine	20 mg Thiamine HCl
20 g L-Histidine	20 mg Nicotinic acid
40 g DL-Tryptophane	40 mg Pyridoxamine
20 g L-Arginine	4 mg *p*-Aminobenzoic acid
10 g L-Lysine	0.04 mg Biotin†
20 g Aminoacetic acid	

* Total mix contains 2289 g, sufficient for 100 l of assay medium.

† This small amount of biotin may be conveniently incorporated in dry form in the mix by mixing 0.4 ml of a stock solution of biotin containing 0.1 mg of biotin per ml with 5 ml of a water solution containing 1 g of the 20 g of DL α-alanine required in the final mix, and evaporating to dryness on a water bath.

which should give a transmission of 25 on an Evelyn photoelectrometer with 520 mμ filter, is transferred to each liter of liquefied assay medium, precooled to 52° C.

Inoculated medium is distributed into flat-bottom Petri dishes in 25-ml quantities and allowed to harden. Assay cylinders are then placed on the agar surface and the dishes stored at 4° C until needed. Solutions containing 0.03, 0.05, 0.1, 0.2, 0.4, and 0.6 μg B_{12} per ml, M/50 pH 5.2 Na_2HPO_4-KH_2PO_4 buffer are prepared for daily determination of a standard curve. Check standard solution containing 0.2 μg B_{12} is included on assay plates, in addition to unknowns diluted to approximately this level with M/50 buffer. Three assay cups are filled with standard solution and three alternate cups with unknown solution in each Petri dish.

After 18-hr incubation at 37° C, diameters of growth zones are measured and calculations made in the same manner used for antibiotic assays. A typical assay yields 1.8-mm growth zone diameter increase for each twofold increase of B_{12} concentration and approximately 17-mm growth zone for the 0.2-μg check standard.

Standard deviation (66% confidence limit) for the cup assay is ±10% as compared with ±21% for the titrimetric assay, with similar replication and the same assay organism.[2]

[2] One cup assay is calculated from the average diameter of three zones of solution under test and three zones of standard solution on a single Petri dish. One titrimetric assay is the averaged value from five assay tubes at different concentration gradients, compared with 20 tubes containing standard solution at concentration gradients.

By the cup technique, *L. lactis* shows no response to thymidine, desoxyribonucleic acid, or 0.5% ascorbic acid. Response is obtained with crystalline vitamin B_{12}, vitamin B_{12a} (*7*), liver concentrates, and certain microbiological fermentation products. The fermentation materials frequently require autoclaving to destroy associated antibiotics, or acidification for release of LLD growth-promoting factors from the cells. Insoluble adsorbates, and fermentation residues, often yield full activity following suspension in water and apportioning the suspension directly into assay cups, although supernatant liquors from such suspensions may contain little growth factor.

In order to obtain full LLD activity with some adsorbates, such as APF adsorbates, it is necessary to dilute suspensions to 0.05 μg B_{12} equivalent per ml. For these samples, the check standard solution should also contain 0.05 μg B_{12} per ml.

In the cup assay described, quantitative values are assigned to the growth response of *L. lactis* Dorner (A.T.T.C. No. 10,697) to unknown preparations on the basis of an assumed value of 11×10^6 activity units per mg of vitamin B_{12}. To distinguish from the Shorb LLD unit (*11–13*), the unit of *L. lactis* Dorner activity as determined by the herein-described cup method is designated as the LLDCC unit of LLD type activity. The cup assay shows no LLD response to desoxyribonucleic acid or its constituent nucleosides, whereas the Shorb titrimetric assay shows LLD activity for these substances. Cup and titrimetric assays show somewhat different responses to modified substances, such as vitamin B_{12a}, when assayed against a vitamin B_{12} standard. Impure materials, containing various LLD-active substances, do not necessarily yield equal results by both methods. Shorb's liver concentrate standard, assigned a value of 1,000 LLD units per mg, from which the above-noted LLD activity of B_{12} was determined by titrimetric assay, was found experimentally to contain 1,120 units/mg by the cup assay with crystalline vitamin B_{12} standard.

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Note: Description of a cup assay for the antipernicious anemia factor, in which thymidine and related compounds caused interference, was presented orally by Dr. W. F. J. Cuthbertson before the Biochemistry Society in London, January 22, 1949.

Aureomycin in the Cultivation of *Endamoeba histolytica*[1]

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Three attempts have been made to establish a single strain of *Endamoeba histolytica* in Shaffer-Frye medium (*3*) containing aureomycin in place of other antibiotics. The aureomycin (Duomycin) was obtained from Lederle Laboratories in vials each containing 50 mg of powdered aureomycin. This was diluted in a phosphate buffer, pH 6.9, and used within 2 hr. Final concentrations of aureomycin in the culture tubes ranged from a dilution of 1:1,000 to 1:5,000,000.

In each experiment the inoculum used consisted of 48-hr cultures of the amebae collected in large numbers by centrifuging the buffered saline overlay containing rice starch from flasks of coagulated egg base (*2*). These flasks were inoculated with amebae from Balamuth's culture medium (*1*). Counts were made on the material inoculated into the aureomycin cultures, and a volume of 0.5 ml was inoculated into each tube. Growth of the amebae in culture was estimated by examining them through the wall of the test tube placed under the 16-mm objective of the microscope and recording the relative numbers in terms of 0, ±, +, ++, +++, or ++++.

In the first attempt to establish our human strain XXII in the aureomycin cultures, five dilutions of aureomycin were used with two tubes for each dilution, and four control tubes were set up, two having 10,000 units of streptomycin and 5,000 units of penicillin in 0.5 ml of buffered saline, and two having the same amounts of streptomycin and penicillin in 0.2 ml of physiological saline. The aureomycin dilutions used were 1:1,000, 1:2,000, 1:10,000, 1:100,000, and 1:1,000,000. Transfers of the cultures were made at 48- or 72-hr intervals.

In this first experiment, positive cultures were obtained only in the tubes containing aureomycin diluted 1:100,000 and 1:1,000,000, and in the controls. The two 48-hr cultures of 1:1,000,000 dilution (++++ growth) were pooled and from them tubes containing aureomycin diluted 1:33,000, 1:50,000, 1:1,000,000, and 1:2,000,000 were inoculated. Growth was obtained in all dilutions, but it was decidedly better in the 1:1,000,000 and 1:2,000,000 than in the lower dilutions. The two tubes containing the 1:33,333 dilution remained positive only 48 hr and those containing 1:50,000 remained positive 72–96 hr. One tube containing 1:2,000,000 was positive 168 hr after inoculation. A third passage was made 72 hr after the previous transfer and positive cultures in dilutions of 1:50,000, 1:100,000 (inoculum 120 hr old), 1:1,000,000, and 1:2,000,000 were transferred. Only two tubes became positive for amebae and they had a ± rating 48 hr after inoculation. After the third transfer the

[1] Supported by a grant-in-aid from the National Institutes of Health, Bethesda, Md. Thanks are due Dr. Herald Cox, Lederle Laboratories, Pearl River, N. Y., for furnishing supplies of aureomycin and important data on its properties.

control tubes also were negative except for one ± tube 24 hr after inoculation.

In this first attempt to establish the amebae in aureomycin cultures, the tubes containing aureomycin dilutions of 1:1,000 and 1:2,000 were clear but decidedly yellow, due to the high concentration of aureomycin. The other tubes were moderately turbid and became increasingly so with age. After the second transfer all tubes were considerably less turbid than before, but did not become perfectly clear until after the third transfer. When the third passage was made, tubes of brain heart infusion and thioglycolate media were inoculated with the amebic cultures to test for living bacteria. The tubes inoculated from the control cultures remained clear (presumably negative for bacterial growth) for 96 hr, when they were discarded. The tubes inoculated from the aureomycin cultures all became cloudy (positive for bacterial growth), but the inocula containing aureomycin dilutions of 1:33,333 and 1:50,000 showed slower growth of bacteria than did those in dilutions of 1:100,000 and higher.

In a second attempt to establish the amebae in aureomycin cultures, this antibiotic was used in six dilutions: 1:33,333, 1:100,000, 1:333,333, 1:1,000,000, 1:2,000,000, and 1:5,000,000. Four controls with streptomycin and penicillin were set up as before. The first passage of the amebae into the aureomycin medium resulted in positive cultures in all dilutions, but the 1:33,333 dilution was negative after 48 hr. Growth in the 1:100,000 dilution was best at 24 hr and decreased steadily thereafter, while in all the higher dilutions ++++ growth was recorded after 48 hr. All tubes were quite turbid in 24 hr, the 1:5,000,000 dilution having the greatest turbidity.

In this experiment the amebae were maintained through five serial passages made at 48-hr intervals. In one set of tubes, transfer of the amebae was made into tubes containg the same dilution of aureomycin as previously, while in a second set the positive cultures remaining after the third passage were transferred into media containing the next highest dilution of aureomycin in series. In this second set of cultures, four tubes were inoculated containing aureomycin in dilutions of 1:333,333, 1:1,000,000, 1:2,000,000, and 1:5,000,000. The last dilution was turbid in 24 hr and did not become positive for amebae, while the other three cultures were positive after 24–48 hr but were very poor and showed gas production. The four cultures were transferred one more time into the same aureomycin dilutions but only one tube showed growth, the 1:2,000,000, which remained ± for 72 hr before becoming negative.

In the series of cultures which were transferred into the same dilutions of aureomycin, the amebae in the dilution of 1:33,333 did not survive a second passage. The amebae in the 1:100,000 dilution survived four passages before dying out, but did not grow quite as well as those in the higher dilutions. In the 1:333,333 dilution, the amebae grew quite well at first but died out after the fourth passage. Amebae in the dilution of 1:1,000,000 remained positive through five passages when they were discontinued, since growth at that time was very poor. After the second passage, the tubes having the 1:5,000,000 dilution of aureomycin became very turbid, and the 1:2,000,000 dilution increased in turbidity. Gas production was evident in the 1:2,000,000 tubes after the third passage, in the 1:1,000,000 and 1:333,333 tubes after the fourth passage, and in the 1:100,000 tube after the fifth passage. In the control cultures with this series, only two of the four survived the third passage, one the fourth, and none the fifth.

A third attempt was made to establish the amebae in aureomycin cultures, starting this time with four dilutions: 1:100,000, 1:500,000, 1:1,000,000, and 1:2,000,000. Only two controls were run, using 10,000 units of streptomycin and 5,000 units of penicillin in 0.5 ml of buffered saline. The control tubes were negative for amebae after the third passage, and were discontinued. Six serial passages were made with the aureomycin cultures, and the only one which survived them all was the 1:1,000,000 dilution, which became negative 48 hr after the last transfer. The growth of the amebae was poorer in the 1:100,000 dilution than in the higher dilutions and became negative earlier, surviving only four passages. There was little difference in the amount of growth obtained in the other three dilutions; however, the 1:2,000,000 dilution had a tendency to become turbid when kept four or five days. Gas production was never eliminated from those tubes in which the amebae grew.

As in the second experiment, these cultures were transferred following the first passage to media containing the next higher dilution of aureomycin and maintained in the decreased aureomycin concentration. There was no significant difference in the growth or survival of amebae in the dilutions of 1:500,000, 1:1,000,000, and 1:2,000,000; however, when the amebae in 1:2,000,000 were put into a dilution of 1:4,000,000, the medium became so turbid that this dilution was not continued. In the other three dilutions, the amebae survived four and five serial passages.

From the experiments described it seems that there is an optimum range of aureomycin concentration for the growth of *E. histolytica*. Too high a concentration, or a dilution of less than 1:100,000, appears to inhibit amebic growth, either directly or indirectly, although bacterial growth may be checked or inhibited. Too great a dilution, 1:2,000,000 or more, is insufficient to control bacterial growth and therefore unsatisfactory as a substitute for penicillin and streptomycin. Within a certain range, possibly 1:300,000 up to 1:1,000,000, the amebae grew well but there was evidence that bacterial growth was not inhibited. On the basis of these experiments, it would appear that the strain of amebae tested grows in the aureomycin cultures as well as, if not better than, in the penicillin-streptomycin cultures, although control of bacterial flora was less satisfactory.

References

1. Balamuth, W. *Amer. J. clin. Path.*, 1946, **16**, 380.
2. Shaffer, J. G. and Frye, W. W. *Amer. J. Hyg.*, 1948, **47**, 214.
3. Shaffer, J. G., Ryden, F. W., and Frye, W. W. *Amer. J. Hyg.*, 1948, **47**, 345.

Comments and Communications

The Structure and Activity Relationships of the Choline Group of Drugs Determined by Measurements of Phase-Boundary Potential

The interesting paper of Ing (*Science*, 1949, **109**, 264) presents data exposing discrepancies in the proposal made by Pfeiffer that muscarinic action is produced by a spatial molecular configuration (*Science*, 1948, **107**, 94). Both authors have pointed out pharmacologically important features of the structural formulas of cholinergic substances but no mention is made of the lipoid solubility or electrogenic properties of the compounds described.

Twenty years ago, the senior author (Beutner, R., *J. Pharm. exp. Therap.*, 1927, **31**, 305) reported the outstanding phase-boundary potential of alkaloids and recently the transient potentials (waves) of acetylcholine were described (Seventeenth International Congress of Physiology, Abstracts of Communications, p. 390, 1947; Second International Congress of Electroencephalography, Paris, 1949). These investigations of the essential or electrical action of cholinergic drugs show that pharmacodynamics must deal with energy relationships and attempt to discover the mechanism underlying the relation of structure to action. We have measured the phase-boundary potentials of choline and acetylcholine and also determined the ohmic resistance of the oils shaken with choline and acetylcholine. Acetylcholine chloride, at a concentration of 0.0027 M, produced 35 mv negativity at the interface between saline and guaiacol, reducing the resistance from 2.4×10^6 to 2.7×10^5 ohms. In the same apparatus, 0.0027 M choline chloride produced only 5 mv negativity, and reduced the resistance of the oil from 2.4×10^6 to 8.0×10^5 ohms.

These data throw light on the mechanism of action of this type of drug. Acetylcholine is a stronger cholinergic drug because it penetrates into the lipoid, and because after penetration it ionizes in the nonaqueous phase. For these reasons there is a higher ion concentration in the lipoid at the site of contact with acetylcholine. This in turn entails a larger negative potential at the lipoid surface. Such a variation is the essential factor in nerve activity. Changes in these physical properties are produced by the introduction of acetyl groups in choline, as our data show. Ing assigns special significance to the size of the "cationic head" of a cholinergic drug and to the charge on the N- atom. Without doubting the justification for these assumptions, we believe that these are factors influencing ionization in the lipoid phase and consequently of secondary importance for the pharmacological effect. The influence of the exchange of ethyl for methyl groups in acetylcholine would likewise exert pharmacological effect primarily through influence on the electrogenic properties of acetylcholine, and this holds also for other substitutions.

We agree with Ing that the term *prosthetic* applies to the acetyl group. In conclusion, it would appear that the "cationic head" of Ing, the "prosthetic groups" of Pfeiffer, and the "positive charge on the central nitrogen" of Taylor (*Nature*, 1947, **159**, 86) are nothing more than ionization factors in the phase-boundary potentials of alkaloids previously described (cf. Beutner 1927).

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Geological Applications of Short Range, Two-Way Radio Sets

Recent success with portable, short range, two-way radio sets ("walkie-talkie") in instruction of students in field geology suggests many possible applications of this or similar devices in educational and professional work.

The short range two-way radio, designed for voice conversation, is described in the War Department's Technical Manual No. 11-235, May 14, 1943, pp. 2–4 as a press-to-talk, portable, radio telephone, receiving and transmitting on the same frequency. The total weight of the set, including batteries, is 5.5 lb. The radio receiver is battery-powered; batteries should last about 15 hr under almost continuous operation.

Graduate field courses in geology, conducted as a part of the regular curriculum of class work at Louisiana State University, have for some time posed a problem in how to instruct these students properly in the field. These classes, in many instances, travel long distances between individual outcrops or type areas. Geologic and geomorphic features of considerable importance in student training often are present between such localities. In order to provide properly trained personnel for each car participating in these class trips, the enrollment previously has been restricted to a number sufficient to fill two cars. The increased graduate enrollment of the last few years, and the consequent increased demand for this type of course, has resulted in classes too large for proper instruction.

Recently, the technique of equipping each car with a portable, short range, two-way radio set was tried. Six cars and 24 students participated. One staff member, acting as trip leader, rode in the lead car; by means of the radio telephone he gave directions and instructions, and kept up intermittent discussions of various features encountered between the individual stops.

Signals for communication between cars were given by white flags or horns. In areas of sufficient interest, sets were kept on constantly; otherwise they were shut off until flags signaling communication were flown.

To overcome shielding and absorbing of signals by the metals in the car, aerials were extended outside the cars at all times during communication. For similar reasons, it was necessary to prevent contact of the aerial with the metals of the car.

The considerable success attained with this technique in so large a group allows for similar and related uses in field parties of various kinds. Such applications can be applied easily to almost any type of field investigation or construction operation utilizing more than one man.

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Longevity of the Tropical American Toad, *Bufo marinus* L.

Though toads are known to live for many years, there are few published records detailing the methods under which longevity tests have been conducted. In the experiment described here the toads were confined in a cage 8 ft long, 4 ft wide, and 2 ft high. It was covered with strong, galvanized screen of 1/8-in. mesh, attached to a heavy framework of concrete posts. Iron sheeting, 1 ft wide, was imbedded vertically in the ground just inside the walls to a depth of 6 in. This was to prevent any possibility of toads' burrowing out. A strong door, provided with a padlock, was built in the top of the cage.

To get toads for the test, eggs were collected on May 26, 1933, from a reservoir near Honolulu, where a female *Bufo*, attended by a male, had been observed laying an egg string. Some of the eggs were placed in a pan of water and hatched on May 29. The larvae were given green algae and boiled rice, on which they thrived. Metamorphosis was completed by June 30 and the toadlets, measuring about 6 mm in length, were placed in the cage. The ground was kept wet, and the cage was partially shaded. A small brick-lined retreat was constructed in one corner. Quantities of ants were supplied for food at frequent intervals. Within a few weeks the toads had grown sufficiently to take larger insects, and by October 1, when they were 3 months old, they were from 2½ to 3 in. long and able to swallow almost any insect given them.

The experiment started with 26 toads. By the time they were 6 months old, when many of them had reached a length of 4 in., the problem of feeding them sufficient insects became acute. The population was thinned to nine toads, consisting of five females and four males. By setting appropriate traps, cockroaches were caught to feed the toads. Many hundreds of roaches were placed in the cage weekly. A large pan of water was also supplied, but none of the confined toads ever laid any eggs.

This experiment continued until May 14, 1949, when the last toad—a large female—died, after being under almost daily observation for 15 years, 10 months, and 13 days. She had consumed during her lifetime, according to our estimate, about 72,000 cockroaches. The other eight toads in the test had lived from 8½ to 14 years.

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Some Problems in Sensory Prosynthesis

There is at present a very considerable amount of interest in devices by which lost senses can be replaced or at least compensated for. At the Massachusetts Institute of Technology the authors have been working on a method of replacing hearing by tactile stimulation. In this method a sound is carried from a microphone to a bank of filters. The output of each of these filters, except possibly the low frequency stage, is rectified and used to modulate a low frequency carrier and the output of these carriers as well as of the possibly by-passed low frequency stage, is carried to a number of stimulators, which may be properly designed electrodes or may be electromagnetic vibrators resting on suitable points of the skin, such as the five fingers. This produces a pattern of stimulation which we have already proved by experimentation to possess a high degree of recognizability and which we hope ultimately to embody in a portable apparatus by which we expect that the totally deaf can participate in active speech.

In designing this apparatus we have first had to convince ourselves by the theory of the Vocoder that the amount of information which could be transmitted by this transmitter, on the basis of acoustical speech, was of sufficient magnitude to furnish an adequate basis for the understanding of words. We then worked on the principle that in using an inferior sense, such as touch, it was necessary to cut the incoming information to that which is semantically sufficient so as not to overload the receptors of the skin and prolong the learning period. In doing this we have had to transfer part of the cortical function of the ordinary hearing mechanism to an electrical system outside the body. The severe limitation of the amount of information which exists when one tries to transfer one of the cortical functions to an external machine should be a guiding principle in other sensory replacements, such as those for the blind.

It is most important in all such prosthetic apparatus that the patient should not separate the problem of active communication, such as speech, from that of passive communication, such as hearing. In the normal individual, speech is maintained at a high level only by the continual monitoring of the speaking person in which, at no time, is he unable to compare his own speech with that of others. This is equally important, or even more important, in artificial methods of communication such as we are devising. The portability of the apparatus is not an advantage, but it is a necessity.[1] Under these conditions, as we have already demonstrated experimentally, the patient immediately begins to improve the quality of his speech by comparison and his voice begins to lose its deaf-mute deadness.

We suggest these principles as a basis for further work in sensory replacement.

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[1] The importance of feedback in the learning process is discussed at length in the book *Cybernetics* by Norbert Wiener, published by John Wiley & Sons. The apparatus employed in the course of the research reported above is described in the December 15, 1948 *Quarterly Progress Report* of the Research Laboratory of Electronics, Massachusetts Institute of Technology.

Scientific Book Register

BOCHNER, S., and CHANDRASEKHARAN, K. *Fourier transforms.* Princeton, N. J.: Princeton Univ. Press; London: Geoffrey Cumberlege, Oxford Univ. Press, 1949. Pp. 219. $3.50.

BOIES, LAWRENCE R. *et al. Fundamentals of otolaryngology: a textbook of ear, nose and throat diseases.* Philadelphia-London: W. B. Saunders, 1949. Pp. xv + 443. (Illustrated.) $6.50.

DAVENPORT, HORACE W. *The abc of acid-base chemistry: the elements of physiological blood-gas chemistry for medical students and physicians.* (2nd ed.) Chicago: Univ. Chicago Press, 1949. Pp. 78. (Illustrated.) $2.00.

DAVIS, TENNEY L. (Ed.) *Chymia: annual studies in the history of chemistry.* (Vol. 2.) Philadelphia: Univ. Pennsylvania Press, 1949. Pp. x + 143. (Illustrated.) $4.00.

DE KRUIF, PAUL. *Life among the doctors.* New York: Harcourt, Brace, 1949. Pp. 470. $4.75.

FIELD, HENRY. *The anthropology of Iraq: the lower Euphrates-Tigris region.* (Part I, No. 2, Publ. 631). Chicago: Field Museum of Natural History, 1949. Pp. 227 + 426, plates 49 + 228. (Illustrated.) $5.00.

FLOSDORF, EARL W. *Freeze-drying: drying by sublimation.* New York (18): Reinhold, 1949. Pp. vii + 280. (Illustrated.) $5.00.

Gmelin's Hanndbuch der Anorganischen Chemie. (8th ed., System No. 10-B, Selenium.) Clausthal-Zellerfeld, Germany: Gmelin-Verlag, GMBH, 1949. (U. S. distributor: Dimitri R. Stein, 105 Pinehurst Avenue, New York (33), N. Y.) Pp. xxviii + 195. (Illustrated.) $16.25.

KLOEFFLER, ROYCE GERALD, and HORRELL, MAURICE WILSON. *Basic electronics.* New York: John Wiley; London: Chapman & Hall, 1949. Pp. xi + 435. (Illustrated.) $5.00.

MAYALL, R. NEWTON, and MAYALL, MARGARET L. *Skyshooting: hunting the stars with your camera.* New York: Ronald Press, 1949. Pp. xi + 174. (Illustrated.) $3.75.

MOORE, CHARLOTTE E. *Atomic energy levels: as derived from the analyses of optical spectra,* Vol. I, ^{1}H–^{23}V. (National Bureau of Standards Circular 467.) Washington 25, D. C.: Supt. of Documents, U. S. Govt. Prntng. Office, 1949. Pp. xliii + 309. $2.75.

ORDWAY, SAMUEL H., JR. *A conservation handbook.* New York (16): Conservation Foundation, 1949. Pp. 76. $1.00 postpaid.

PALMER, RALPH S. *Maine birds.* (Bull. Museum of Comparative Zoology, Harvard College, Vol. 102.) Cambridge 38, Mass.: Museum of Comparative Zoology, 1949. Pp. 656. $5.00.

RIDER, PAUL R. *First-year mathematics for colleges.* New York: Macmillan, 1949. Pp. xv + 714. (Illustrated.) $5.00.

NEWS and Notes

Alexander Spoehr, curator of oceanic ethnology, has left for a year's anthropological research for the Chicago Natural History Museum on Saipan and the Marianas. The expedition is sponsored by the National Research Council, in cooperation with the Navy Department. Dr. Spoehr will study the cultural change among the natives of the islands and conduct excavations in the Marianas to determine how these islands were originally peopled.

Thomas J. Parmley, professor of physics at the University of Utah and consultant at the Radiation Laboratory of the University of California, has joined the staff of the x-ray laboratory, Atomic and Molecular Physics Division, National Bureau of Standards. Dr. Parmley will investigate methods for measurement of the intensity and special distribution of pulsed x-rays.

Grant Taylor, assistant dean of the Duke University Medical School, has been named deputy director of the Atomic Bomb Casualty Commission in Japan. Dr. Taylor, who is associate professor of pediatrics and bacteriology at Duke, has been granted a two-year leave of absence for the special assignment.

Roger S. Warner, who recently resigned as director of engineering for the Atomic Energy Commission, has joined the staff of Arthur D. Little, Inc., research and engineering organization of Cambridge, Massachusetts.

Henry C. Meadow, coordinator of industrial research at the University of Rochester, has been appointed executive secretary to Harvard University's Committee on Research and Development for Medicine and Health. The committee is charged with the responsibility of coordinating the appeals for support of research and advanced training in all branches of science related to medicine and health.

Thorkild Jacobsen, director of the Oriental Institute and dean of the Division of Social Sciences at the University of Chicago, left for Baghdad October 27 with Mrs. Jacobsen, to join the University of Chicago-University of Pennsylvania archaeological expedition in Iraq. The group will continue excavating begun 50 years ago in the ruins of Nippur, 100 miles south of Baghdad.

Thomas J. Kirwin, assistant director of the James Buchanan Brady

Foundation for Urology, New York Hospital, has been appointed professor of urology at New York Medical College and director of the Department of Urology, Flower and Fifth Avenue Hospital and Metropolitan Hospital.

Visitors

H. Heller, professor of pharmacology of the University of Bristol, and **Hans Selye,** professor of physiology at the University of Montreal, were guest speakers at the University of Texas Medical Branch, Galveston, November 4 and 8 respectively. Professor Heller discussed the influence of renal factors on blood pressure, and Professor Selye, the alarm reaction.

Recent visitors at the National Bureau of Standards were: **J. J. W. den Haan,** chief engineer, Philips Research Laboratories, Eindhoven, Netherlands; **Adrien Jaquerod,** director, Swiss Laboratory of Horological Research, Neuchâtel, Switzerland; **P. W. Kim,** director of Technique and Supply, Kyongsong Spinning Company, Ltd., Seoul, Korea; **O. H. C. Messner,** consulting engineer, Gut Rosenberg, Zurich, Switzerland; **Ralph B. Watts,** head of Science Department, Australian Missionary College, Cooranbong, N.S.W., Australia; **P. Alexander,** manager, Research Department, Wolsey Ltd., Leicester, England; **A. T. S. Babb,** senior physical chemist, J. Lyons and Company, Ltd., London.

Grants and Awards

The 1950 medal of the Industrial Research Institute will be presented next April to Frank B. Jewett, former president of the National Academy of Sciences and for many years vice president of American Telephone and Telegraph Company. The medal is presented annually for "outstanding accomplishment in leadership or management of industrial research which contributes broadly to the development of industry or the public welfare."

Norten C. Melchior, assistant professor of biochemistry at the Stritch School of Medicine, Loyola University, Chicago, has been awarded a grant-in-aid from the Permanent Science Fund of the American Academy of Arts and Sciences for the study of metal-organic complex compounds.

The 1949 Nobel prize for medicine was awarded jointly to a Swiss and a Portuguese for their work with human and animal brains, the physics prize went to a Japanese-born professor at Columbia University, and the chemistry prize to a Canadian-born professor at the University of California.

Walter Rudolf Hess, 68, director of Zurich University's Physiological Institute, and *Antonio Caetano de Abreu Freire Egas Moniz,* 75, professor emeritus of neurology in the Faculty of Medicine of the University of Lisbon, shared the prize money for physiology and medicine. Dr. Hess, a specialist in the circulation of the blood and breathing, was recognized for his experiments on cats and dogs showing how certain parts of the brain control the organs of the body. Dr. Moniz received the award for his development of the surgical technique known as prefrontal lobotomy, for the treatment of schizophrenia and paranoia.

Hideki Yukawa, 42, visiting professor of theoretical physics at Columbia University since last September, won the physics prize "for his prediction of the existence of the meson (an elusive mass, heavier than the electron, which theoretically glues the atomic nucleus together), based upon his theory of nuclear forces." Dr. Yukawa was only 28 and a recent graduate at the University of Kyoto when he first predicted the existence of the meson.

William Francis Giauque, 54, professor of thermodynamics at the University of California, received the prize in chemistry "for his contribution to chemical thermodynamics, especially for his investigations of the properties of substances at extremely low temperatures." Through Dr. Giauque's methods, temperatures have been pushed within a few thousandths of a degree Kelvin of absolute zero.

The Nobel prizes, which have been awarded annually since 1901, will be presented at a ceremony in Stockholm on December 10. The peace prize will go to Lord Boyd Orr, as reported in *Science* October 28. No prize in literature will be awarded this year.

The Research Corporation has awarded a grant to Martin B. Williamson, assistant professor of biochemistry at the Stritch School of Medicine, Loyola University, Chicago, for the study of the chemical structure of proteins.

Colleges and Universities

The Saint Louis University Department of Biology has inaugurated a program of graduate research leading to advanced degrees in Arctic biology. In addition to laboratory research, the program will include field work in Alaska, under the direction of Charles G. Wilber, head of the department. A grant of $9,000 from the U. S. Air Force will assist the program.

University of Rochester scientists have developed a new motion picture camera lens made from artificial sapphire which has several advantages over optical glass lenses. Its extreme hardness makes it almost impossible to scratch, and its high refractive index, which changes very little with the color of the light, improves the sharpness and quality of the images produced.

Meetings and Elections

At their recent meeting at Woods Hole, Massachusetts, the **Atlantic Fisheries Biologists** elected William R. Martin and Frank D. McCracken of the Fisheries Research Board of Canada, St. Andrews, New Brunswick, as president and secretary-treasurer respectively.

The American Chemical Society will hold its 16th annual chemical engineering symposium in Columbus, Ohio, December 29 and 30 at the Ohio State University. The symposium, which will be under the direction of a committee headed by E. W. Thiele, of the Standard Oil

Company, will deal with every aspect of material transfer between a gas and liquid phase, or between two liquid phases. J. H. Rushton, of the Illinois Institute of Technology, is chairman of the technical program.

An International Colloquium on Adsorption and Heterogenous Kinetics, sponsored by the French National Center of Scientific Research, was held at the University of Lyon, France, September 12–17. The meeting was organized by Marcel Prettre, head of the Department of Industrial Chemistry of the University of Lyon, and was attended by about eighty scientists from various countries including the United States, Great Britain, Austria, Belgium, Holland, Australia, and France.

Visiting scientists who presented papers at the meeting were H. S. Taylor (Princeton) and P. H. Emmett (Mellon Institute); R. M. Barrer (Aberdeen), S. R. Craxford (British Fuels Research Laboratory), B. M. W. Trapnell (Royal Institute), and A. R. Ubbelohde (Belfast); J. Jungers and E. Mertens (Louvain); C. Herbo (Brussels); H. Forestier (Strasbourg); and E. Cremer (Innsbruck). French scientists participating included M. Prettre, R. Bernard, C. Courty, M. Perrin, Y. Eyraud, J. Sanlaville, P. Besson, S. Teichner, A. Troesch, P. Cornuault, E. Pernoux, and Y. Trambouze (Lyon); N. Bauer, M. Magat, M. Haissinsky, J. M. Dunoyer, M. Mathieu, M. Mering, J. Longuet-Escard, J. Escard, and Miss F. Fouinat (Paris); A. Michel (Lille); G. Valensi (Poitiers); and A. Guillemin, J. Vincent-Genod, J. Givaudon, E. Nagelstein, and R. Leygonie (French Petroleum Institute at Paris). In addition to those mentioned above, a number of visiting scientists from England, Holland, Belgium, and France took part in the discussions. In this group were C. Kemball, of Cambridge University, and the well-known catalytic chemist, L. Andrussow.

The meeting was opened by addresses of welcome by Prof. Douin, dean of the Faculty of Science at the university and by Prof. Prettre. At the same time M. Magat, who acted as official interpreter, was introduced to the colloquium. Prof. Magat, with his fluent command of French, English, and German and his well-founded and broad grasp of modern physical chemistry, contributed greatly to the success of the conference by his rapid and accurate translation of all discussions into French and English.

An interesting program of some forty papers that followed was divided into three main groups dealing with (1) the physical and chemical adsorption of gases by solids, (2) the texture and structure of catalyst surfaces as revealed by x-ray, adsorptive, electron microscopic, and magnetic techniques, and (3) the theoretical and experimental study of heterogenous kinetics of gas-solid and liquid-solid systems. According to present plans all of the contributed papers, together with the discussions, are to be published in a future issue of one of the French journals; accordingly, further details of the program will not be presented here.

The warm hospitality of the French hosts made the meeting especially pleasant for the visiting scientists. At the start of the meeting they were welcomed by a reception at the Hotel de Ville by a representative of M. Herriot, mayor of Lyon, and former prime minister of France. Throughout the week a series of luncheons and dinners gave all of us a chance to praise the excellent cuisine for which Lyon is noted and at the same time afforded an opportunity to discuss informally many matters of mutual interest.

PAUL H. EMMETT

An International Colloquium on Macromolecules was held September 1–5 in Amsterdam, Holland. The meeting, organized by Hermans, Koenigsberger, Overbeek, and Staverman had been very well prepared (all participants received a complete set of preprints about three weeks before its start) and gave an excellent cross section through recent progress in polymer kinetics and in the statistical treatment of macromolecules in solution. A number of papers on polycondensation, radical, cationic and anionic catalyzed addition polymerizations (by Champetier, Evans, Magat, and Melville) demonstrated that the kinetics of the formation of macromolecules under very widely varying conditions is beginning to be understood in a quantitative way. The trend now seems to be to apply the present results to arrive also at a quantitative control of copolymerization and to find ways and means to synthesize macromolecules of still higher molecular weights.

Particular interest was shown in several papers, by Eirich, Hermans, and Putzeys, on the statistical treatment of coiled macromolecules in solution and on the scattering of light by them. A series of contributions by Katchalsky, Künzle, and Overbeek was devoted to polyelectrolytes, with special emphasis on the significance of this branch of polymer science for the chemistry of proteins.

The level of all presentations was remarkably high; there was plenty of time for discussion and excellent use was made of it. On several fundamental points there was definite disagreement between the leading contributors, which resulted in animated discussions and arguments. The spirit and the stimulating effect of this colloquium were reminiscent of High Polymer Week at the Gordon Conference in Colby College. A volume containing all presentations and discussion remarks is scheduled to appear in about three or four months.

H. MARK

Conference on the Gene. A conference for examination of current developments and trends in studies of the gene was held at Shelter Island from May 30 to June 2 under the sponsorship of the National Academy of Sciences. The group of 20 participants included well-established geneticists and younger workers in the field. Free and informal discussion characterized the meetings, and provided an atmosphere conducive to critical examination of various aspects of the gene problem. The topics discussed included the mechanism of reverse mutation, the nature of allelism, the gene-enzyme relationship, the evidence for recom-

bination in bacteria and bacteriophages, the role of the cytoplasm in heredity, and the chemical nature of chromosomal materials. There was general agreement among participants that these meetings in a quiet and congenial atmosphere provided opportunities such as are rarely encountered in large, formal meetings, for critical evaluation and integration of genetic studies on a variety of organisms. In the opinion of the participants, the conference exerted a directional influence that will be reflected in future studies of gene structure and function.

BERWIND P. KAUFMAN

A symposium in plasma proteins was held at the University of Illinois College of Medicine September 23–24, under the sponsorship of the Robert Gould Research Foundation of Cincinnati. Eighteen papers were presented by investigators engaged in research in this field in one afternoon and two morning sessions. Junior associates of the speakers were present as guests of the Robert Gould Research Foundation. At the evening session a motion picture was shown by E. V. McCollum, and an address given by Hugues Gounelle of Paris, on some of the unexpected observations during years of underfeeding in France.

Although the subject of the symposium was plasma proteins, the consideration of the subject was purposely so broad that the program included papers dealing with fundamental aspects of protein metabolism which might not ordinarily be considered as falling within the implications of such a title. The program was built around the principal topics of formation, dietary relationships, fractionation of plasma proteins, immunologic relationship, relation to the liver, hypoproteinemia, tracer isotope studies in relation to the plasma proteins, endocrine relationships, and amino acid competitors. Sidney C. Madden spoke on plasma protein formation in disease states and Irving M. London on studies of rates of turnover of plasma protein in man. Fractionation and some of the interactions of the plasma protein were presented by J. L. Oncley, and a discussion of the binding properties of serum proteins for small molecules by S. H. Armstrong, Jr. Tracer and isotope studies included papers by David Shemin on aspects on the biosynthesis of amino acid and proteins, and by Paul C. Zamecnik and Ivan D. Frantz, Jr. on the use of C^{14}-labeled amino acid in the study of peptide bond synthesis. The effect of dietary proteins on synthesis and relations between diet protein stores and plasma protein were presented by Bacon F. Chow and James B. Allison. Hypoproteinemia, particularly in relation to protein starvation in man and its clinical relationships, was discussed by Robert Elman and experimental studies of protein deficiency and temperature in relation to the formation of edema by M. Hegsted. Studies of the fate of intravenously injected plasma albumin were described by Fuller Albright and its metabolism in normal and undernourished individuals by Charles S. Davidson. Clinical studies of the relation of proteins to nutritional edema were presented by Dr. Gounelle. Certain immunological aspects of the plasma proteins were presented by Paul R. Cannon and Michael Heidelberger, and the effect of adrenal cortex on plasma protein formation and utilization and the physiological properties of amino acid antagonists were given by Abraham White and Karl Dittman respectively. Discussion followed each session. The papers will be made available later as a monograph.

JOHN B. YOUMANS

A thriving scarlet ibis colony has been discovered in Venezuela by Paul A. Zahl, New York ornithologist, who, under the sponsorship of the National Geographic Society, has been searching Venezuela's inland river system for the bird's breeding ground (see *Science*, Sept. 16, p. 289). The rookery lies some 125 miles west of San Fernando and covers an area about half a mile long and a quarter-mile wide, on a nearly inaccessible flood plain. "From a distance," Dr. Zahl stated, "its foliage looks as though it were laden densely with blood-red fruit." He estimates the number of adult scarlet ibis at about 5,000.

Recently Received—

List of Publications, U. S. Forest Products Laboratory, January 1–June 30, 1949. Madison 5, Wisconsin.

Some Lower Huronian Stromatolites of Northern Michigan. Eugene S. Richardson, Jr. Fieldiana—Geology, Vol. 10, No. 8. Chicago Natural History Museum.

Medical Mission to Poland and Finland, July 1–August 27, 1948. Abridged report, submitted by Erwin Kohn. Unitarian Service Committee, Inc., 9 Park Street, Boston 8.

Committee on Public Health Relations: A Summary Report of Activities for the Year 1948. New York Academy of Medicine, 2 E. 103 Street, New York 29.

Wissenschaft und Weltbild. January 1949. (Issued quarterly.) Verlag Herold, Vienna.

Second Notice on AAAS Meeting

There are still plenty of New York hotel rooms for the week of the Association's meeting, December 26–31, but early indications of a shortage of single rooms were justified. Miss Sylvia T. Peltonen, Manager, Housing Bureau, New York Convention and Visitors Bureau, 500 Park Avenue, New York 22, who is in charge of room assignments, reported that she had made reservations for the following number of persons, as of November 7:

Statler	691
New Yorker	120
McAlpin	412
Governor Clinton	192
Martinique	195

The Martinique is now completely booked; the Statler has no more *single* rooms. Take advantage of double rooms and make your reservations in parties of two or more if possible. If all Penn Zone hotels should fill up there are excellent hotels nearby, with the same price range.